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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 38.] 1941. [No. 5.

SUMMARY OF RECENT ABSTRACTS.*

IV. TRYPANOSOMIASIS.

General and Epidemiology.

In a statement of the present position of sleeping sickness in the British Tropical African Territories, LESTER (p. 7) discusses the effect of the disease, and of measures of control, on the human and cattle populations. He points out that with the existing fairly close contact between the medical staffs and the natives, it is not likely that any considerable outbreak will long go undetected, and he makes the point that there is a tendency for fly-free areas to become overpopulated and overstocked, and that soil impoverishment and soil erosion are increasing. This will continue unless the spread of tsetse is stopped and new areas are reclaimed. He states that in Nigeria the people tend to live in towns and villages. This may lead to a high rate of infection, but the communities are comparatively easy to protect. In East Africa, on the other hand, the people are more scattered, living in family groups. Infection rates are therefore lower, but protective measures are more difficult, than in West Africa.

HARDING (p. 697), in Nigeria, has attempted to correlate the deaths from all causes with the sleeping sickness incidence in two areas. In the first a close correlation was found, which extended even to infant mortality, an unexpected finding. In the second no correlation was evident, and it is concluded that here the disease was not fatal. The first district lies in the middle of a sleeping sickness belt and there are very free means of communication. The second is on the edge of the belt and is not traversed by main roads or railways. It may be, therefore, that in the first there is considerable multiplicity of strains, not present in the second district, and that this fact may account for the greater virulence of the disease there.

In the course of an experiment lasting four years, CORSON (p. 10) has shown that a strain of *Trypanosoma rhodesiense*, maintained in sheep and antelopes, and transmitted by *Glossina morsitans*, has retained its power of infecting these animals. Though the antelopes varied greatly in their resistance, all the infected animals remained infected

* The information from which this series of summaries has been compiled is given in the abstracts made by the Sectional Editors in the *Tropical Diseases Bulletin*, 1940, Vol. 37. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

long enough for the trypanosomes to have been transmitted many times by tsetse flies if the animals had been living under natural conditions in fly areas.

In Nigeria during 1938 BRIERCLIFFE (p. 694) reports that the sleeping sickness teams examined 378,109 persons, and found 21,073 to be infected [a rate of about 5 per cent.] Other cases were diagnosed at hospitals and dispensaries and in all, over 35,000 cases were discovered during the year. In 1939, however, the Report of the Colonial Development Fund Scheme (p. 695) states that of 485,000 persons examined, 19,855 were found to be infected [a rate of about 4 per cent.]. This is compared with the figures obtained in 1935, when the rate was over 20 per cent. In the Benue Province, however, which had not previously been surveyed, a rate of 6·9 per cent. was found in 1939.

In the Gold Coast, SAUNDERS (p. 397) records percentages of infection varying from 1 to 9 in different areas. About 20 per cent. of the patients have remained positive from one year to the next and have had neither symptoms nor treatment in the interval.

In reporting on sleeping sickness in the Belgian Congo, VAN HOOF (p. 397) shows that in the 10 years preceding 1938 the index of new infections fell from over 1 per cent. to about 0·27 per cent. He gives figures of the persons examined and of the new and old cases under control. DE BRAUWERE (p. 398) gives the FORÉAMI figures for 1938 in the Belgian Congo, and quotes a similar percentage (0·28) of new infections found.

VOGEL and RIOU (p. 8) give figures of cases treated in the French colonies during 1937. Sleeping sickness is serious in the Ivory Coast and in Togo, but in the Cameroons and French Equatorial Africa it is now only feebly epidemic. In the French Sudan, SICÉ and TORRESI (p. 9) show that sleeping sickness is most prevalent in those areas which adjoin the Ivory Coast and French Guinea. It is most common along the Volta Noire, the Bani and the Niger.

KAUNTZE (p. 397) reports that in Uganda in 1938, as in previous years, most cases were found in the West Nile area.

Aetiology.

CORSON (p. 9) has summarized the work he has carried out during the years 1930 to 1938. Two of his conclusions are: (1) It must be very difficult to show a decrease and practically impossible to show complete loss of infectivity to man of a strain of *T. rhodesiense* maintained in sheep and antelopes through *G. morsitans*. (2) A strain of *T. gambiense* maintained in Cercopithecus monkeys by cyclical passages through *G. morsitans* seemed to undergo no change in morphology or virulence during more than four years.

DUKE (p. 11) discusses the three main views on the affinities of *T. rhodesiense*, namely (1) that it is a variant of *T. gambiense*, (2) that it is a human strain of *T. brucei*, and (3) that it is a separate species. Evidence at present available indicates that *T. rhodesiense* is considerably less adapted biologically to man and domestic animals than to wild game. The nature of the mammalian host may influence the pathogenicity of a trypanosome for man—thus, attempts to transmit from antelope to man by cyclically infected flies might fail, whereas similar attempts to transmit the same strain from monkeys might succeed.

KLEINE and KUNERT (p. 702) infected calves with *T. rhodesiense* and then treated them with Bayer 205. The animals were immediately cured, but in controls the trypanosomes remained in the blood for several months, though they were scanty and the calves remained in good condition.

REICHENOW (p. 14) has shown that cultures of *T. gambiense* and *T. congolense* are capable of undergoing incipient development in *G. morsitans* in almost all cases, but that permanent infection of the fly is not more easy to obtain with cultures than with blood forms. Under certain circumstances, however, cultural forms may undergo complete development in Glossina.

LWOFF and CECCALDI (p. 13) have shown that the view of REICHENOW, that strains of pathogenic trypanosomes maintained for years in laboratory animals cannot be cultivated, is wrong. They have succeeded in cultivating *T. gambiense*, under these conditions, in Razgha's medium, by using Liquoïde Roche as anticoagulant, but they note that the blood of some individuals, used in the preparation of the medium, inhibits cultivation, while that of others permits it. CHABAUD (p. 12) has succeeded in cultivating *T. rhodesiense*, *T. brucei* and *T. equinum* in the allantoid membrane of fowl embryo, obtaining better results with citrated than with defibrinated blood. The trypanosomes remained virulent for the mouse. LONGLEY *et al.* (p. 12) have shown that an arsenic resistant strain of *T. rhodesiense* grown in the allantoic cavity of fowl embryo showed no change in either virulence or arsenic resistance after 8 subcultures over a period of 41 days. The technique of culture is simplified and is described, and it is noted that *T. equiperdum*, *T. brucei*, *T. evansi* and *T. hippicum* were also readily cultivated in the same way and maintained their virulence. None of these species was infective for the hatched chick.

STEINFELD (p. 698) has failed in attempts to destroy arsenic resistance in *T. gambiense* by various physical and chemical agents, but reports some reduction of the degree of resistance by repeated exposure of the trypanosomes to 10 per cent. glucose *in vitro*.

DE BORCHGRAVE (p. 406) has found that argoflavin and atebrin, though practically inactive clinically, can remove the infectivity of ordinary and arsenic resistant strains of *T. gambiense* for guineapigs if the drug concentration reaches 2 per 1,000. He also notes that argoflavine has a photodynamic action when used in conjunction with strong light.

In an experiment on the cultivation of trypanosomes in media containing human blood, HAWKING (p. 697) found that there was no evidence of inhibition of growth when blood from a person previously infected was used in the medium. By this technique, therefore, there is no evidence of immunity against a second infection. Trypanosomes have been grown in a medium containing blood in which there were appreciable amounts of Bayer 205.

Transmission.

NASH (p. 15) has studied the ecology of the puparium of *G. morsitans* and *G. tachinoides* in N. Nigeria, where *G. palpalis* is not found. He shows that soil temperature and soil water content vary greatly according to the seasons, and that *G. morsitans* breeds in open woodland in the wet season, in small thickets in the early dry season, and in dense forest islands in the very hot weather. This cycle

corresponds to the seasonal concentration of the adults. The cycle of *G. tachinoides* is not certainly known, but in the early dry season breeding takes place in forest islands and later in river beds; the latter breeding places are destroyed at the onset of the rains. In the hot season pupal mortality is high for *G. morsitans* because of the high soil temperatures of its breeding grounds, but is lower for *G. tachinoides* because it uses mainly the river bed sites. Broadly speaking, however, pupal mortality is high throughout the dry season and low throughout the wet, but in the last month of the rains mortality rises or breeding may cease altogether for a time.

He (p. 696) has shown that it is possible in N. Nigeria so to alter conditions by partial clearing of the islands of forest which normally serve as permanent homes of *G. tachinoides*, that in the hot dry season this fly is exterminated. *G. morsitans*, however, is more resistant to high temperatures and low humidities particularly because it selects resting places with favourable micro-climates, so that complete clearing is necessary for its extermination.

JACK (p. 400) has studied the behaviour of *G. morsitans* in S. Rhodesia. Attraction to man appears to be through the stimuli of movement or scent, but it is pointed out that since regular feeding is necessary for reproduction, man cannot replace animals as the normal host. Dark colours are more attractive to the fly than light colours; black is the best colour and more flies are found on the shady than on the sunny side of a black screen. In traps it is thought that shade, or the appearance of shade, is more important than resemblance to an animal, but the dominant factor determining the reaction to traps appears to be the evaporation rate, since although temperatures are as high in the wet season as in the dry, catches are immensely greater in the dry periods. Hungry flies are attracted to the better illuminated spots in forest, but activity is not confined to hungry flies. He (p. 699) discusses the feeding habits of female *G. morsitans* in relation to the developmental stages of the larvae.

In the French Sudan SICÉ and TORRESI (p. 9) report that the commonest tsetse, by far, is *G. tachinoides*, though *G. palpalis* and *G. morsitans* are also found.

RICHARDS *et al.* (p. 699) have discussed the classification of tropical forest communities, a matter which has its interest for those working on the biology of Glossina.

Clinical.

DE BRAUWERE (p. 398) remarks that in the FORÉAMI service the procedure in diagnosis is first gland palpation and clinical examination, followed by gland puncture. Blood examination is only practised if gland puncture is negative, though some observers hold that a thick blood film is more often positive than a single gland puncture. He records infection in a child aged 10 days; the mother was also infected, and it is suggested that the infection in the child was congenital. CROZAFON (p. 402) prefers to examine fresh rather than stained gland juice, and apart from the triple centrifugation of blood, he regards this as the best method of diagnosis. ROBIN and BROCHEN (p. 402) have found bone marrow puncture to be less useful than the examination of gland juice or blood in the diagnosis of sleeping sickness in all stages of the disease.

SALEUN (p. 403) notes that in French Equatorial Africa a large proportion of cases were diagnosed by the finding of trypanosomes in the cerebrospinal fluid when other methods, for instance gland juice and blood examination, had proved negative. Treatment of early cases, as is usual, was more successful than that of those diagnosed in the later stages.

GEORGIADÈS (p. 402) examined 11 patients with sleeping sickness in whom lumbar puncture was performed. In 7 there was no change in the cerebrospinal fluid attributable to the puncture even if this was repeated two or three times, but in 4 there was an increase in lymphocytes after the first puncture.

KUNERT (p. 17) brings evidence to show that sleeping sickness in the Tabora district of Tanganyika Territory has increased in virulence since 1927. In that year the patients constantly showed enlarged cervical glands, and changes in the cerebrospinal fluid were rare before the third week. In 1938, however, glandular enlargement was rare, and cerebrospinal fluid changes were often found during the first few days. It appears that the trypanosomes now pass quickly through the lymphatic barrier.

LAVIER and LEROUX (p. 401) found pronounced epicarditis, sclerotic endocarditis and periarterial myocarditis, with arteritis of the branches of the coronary vessels, in the hearts of two patients who died of sleeping sickness in the Belgian Congo. The lesions were so extensive that the physiological function of the heart must have been seriously disturbed.

SICÉ *et al.* (p. 18) report two cases of sleeping sickness, in the French Sudan, in which signs of Parkinsonism were seen.

PINARD and BRUMPT (p. 18) record the case of a patient with sleeping sickness who had not lived in Glossina country for 15 years before the onset of symptoms. Either there was a remarkably long latent period or, as the authors surmise, the disease may have been contracted in some other way than through Glossina.

Treatment.

LOURIE and YORKE (p. 404) discuss the trypanocidal action of certain aromatic diamidines, of which 4 : 4′-diamidino stilbene is the most active, giving permanent cures, in mice infected with a laboratory strain of *T. rhodesiense*, in doses of 0·01 to 0·0125 mgm. per 20 gm. weight. The maximum tolerated dose is about 30 times as great as the minimum curative dose. Tests on rabbits in an advanced stage of infection gave equally good results. None of the drugs was effective against *T. cruzi*, *Spirochaeta recurrentis* or *Spirillum minus*, but there is definite action against *Babesia canis* in puppies. DEVINE (p. 700) has studied the effect of 4 : 4′-diamidino stilbene on the blood sugar and blood urea of experimental animals.

DUBOIS and KOHN (p. 701) conclude from experimental work that in animals infected with trypanosomes and treated with Bayer 205, the trypanosomes fix the drug, and that the integrity of the reticulo-endothelial system is not essential for its action.

HAWKING (p. 701) finds great individual variations in the amount of Bayer 205 present in the plasma of persons who have received one or more injections, and recommends that the treatment of Europeans with sleeping sickness should be controlled by chemical estimation of the drug in the blood. In some patients Bayer 205 could be found

in the blood 9 months after the end of the course. Even when present in the blood in considerable quantity, however, it cannot be detected in the cerebrospinal fluid. BOURSNELL and WORMALL (p. 19) found in animals that Bayer 205 is retained in the kidneys longer than in other organs. This retention is of significance in view of the frequent occurrence of albuminuria after administration of the drug in man. The long retention of Bayer 205 in the animal body is due to combination with plasma and tissue proteins.

DE BRAUWERE (p. 398) reports that arsenic resistance is more common in the Belgian Congo than was thought, and three foci were discovered, in which, presumably, a resistant strain of trypanosome exists. Treatment of patients showing arsenic resistant strains is with Bayer 205 and antimonials, and is satisfactory. Ocular troubles resulting from treatment are becoming more rare; tryponarsyl is always used fresh and is dissolved in double-distilled water.

SICÉ (p. 705) writes of the synergic treatment of sleeping sickness with tartar emetic and tryparsamide. Even in cases in which the cerebrospinal fluid was considerably changed when treatment was commenced, the results were good.

KOPP and SOLOMON (p. 705) discuss in detail the untoward reactions caused by tryparsamide. These may be visual, nitritoid or gastro-intestinal, or may affect the skin, brain or peripheral nervous system. COON and ELLIS (p. 406) each report cases in which nitritoid reactions occurred during courses of tryparsamide treatment for neurosyphilis. The condition, which consists of faintness, nausea, flushing, itching of the skin and desire to defaecate, was transient but severe.

Control.

In control LESTER (p. 7) emphasizes the value of mass treatment, which itself will reduce an epidemic to reasonable proportions. With the establishment of dispensaries and with protective clearing by communal labour, mass treatment in Nigeria is the principal measure adopted, and in many of the main epidemic areas the infection rate is now a tenth of the old figure. Movement and concentration of the population is used only as a last resource, and in Uganda and the Sudan, where such movement has been carried out, there is overcrowding and impoverishment of the soil. The report of the Colonial Development Fund Scheme for Nigeria (p. 695) gives details of the methods employed in control. The large decrease in sleeping sickness during recent years has undoubtedly been due more to treatment than to protective measures, but the latter are being steadily pursued and consist of clearings and of settlement schemes. In the latter it is suggested that an allowance of 4·3 acres per head of population should be allowed. DE BRAUWERE (p. 398) points out that in the Belgian Congo the success of treatment is largely due to the fact that the establishment of a large number of dispensaries has made treatment possible in the villages themselves, and that this is greatly preferred by the natives.

In an area of the Gold Coast, however, SAUNDERS (p. 397) attributes mainly to clearings the decrease in the incidence of sleeping sickness.

VAN HOOF *et al.* (p. 703) record experiments in animals on the protective power of Bayer 205. There is no doubt that this drug is an excellent prophylactic, but for use in human communities, where it was hoped that a clean stock of tsetse flies might be developed, the questions of the introduction of trypanosomes from outside, or from

animals (especially pigs), and of ensuring that all members of the community are given the injections, are important. It is desirable to repeat injections at intervals of 3 months.

Chagas's Disease.

Epidemiology.

Mazza (p. 413) reports on 370 cases of Chagas's disease found in the Argentine. Of these, 345 were diagnosed directly by examination of blood in thick drops. He gives a list of the animals found infected in nature, and of the common vectors. Talice and his collaborators (pp. 144, 145) report Chagas's disease from Rio Grande del Sur (Brazil) and from Uruguay.

Aetiology.

Mazzotti (p. 712) has observed variations in virulence in different strains of *Trypanosoma cruzi*. These variations appear to be connected with the different species of Triatomidae in which they were found, or with the locality, so that there appear to be 7 or more strains in Mexico. He (p. 712) finds that the results of inoculation of mice with small numbers of *T. cruzi* are very similar to those obtained when large numbers are employed.

Kolodny (p. 140) has found that if the heart or spleen of young rats infected with *T. cruzi* is removed at the peak of the blood stream infection, and kept in a sealed tube of Ringer or Locke solution, the leishmania stage of the parasite will remain viable for 12 days.

Roubaud and Romaña (p. 413) have shown that *T. cruzi* can survive in fowl embryo for a week, but have not proved that it can multiply.

Transmission.

Brumpt (p. 140) discusses the method of transmission and concludes that although certain workers have reported occasional infections by the bites of infected bugs, the correct explanation is probably that advanced by Yorke, namely that the biting mouthparts have been contaminated with infective faeces. Denecke and von Haller (p. 140), in 52 experiments, failed to produce infection in white mice by the bite of infected bugs. Herr and Brumpt (p. 146) record laboratory infection in Paris from the faeces of an infected bug. The conjunctiva was accidentally contaminated and there followed dacryocystitis, swelling of the same side of the face, enlarged glands and fever. The diagnosis was confirmed by xenodiagnosis, and treatment with a new preparation, Bayer 7602, was followed by subsidence of the fever. Mazza *et al.* (p. 714) report a case of acute Chagas's disease in a child who was bitten near the eye by *Triatoma infestans*. They do not claim that the transmission was effected actually by the bite.

Lent and Pifano (p. 142) name 10 species of Triatomidae found infected in nature. Brumpt *et al.* (p. 141) report natural infection of a number of Reduviid bugs in Mexico, where the disease has not previously been found. Mazzotti (p. 713) gives a list of 15 species of Triatomidae found infected in Mexico. Packchanian (p. 142) has found *T. gerstakeri* to be naturally infected in Texas.

GASIC (p. 414) found infection in 51 per cent. of 1,003 *Triatoma infestans* caught in the Province of Coquimbo, Chile. HOFFMANN (p. 414) reports that *T. flavida*, found only in Cuba, is a potential vector of *T. cruzi*. LENT (p. 713) has found that *Clerada apicicornis*, normally phytophagous, may under certain circumstances suck blood, and that *T. cruzi* is capable of cyclical development in it.

PESSÔA and DE BARROS (p. 143) found that *T. infestans* could be reared at 37°C. in about half the time taken at room temperature, and point out the advantage of this in providing bugs for xenodiagnosis.

Pathology and Clinical.

KOLODNY (p. 143) reports work in which he has demonstrated that immune bodies are present in the milk of rats which have recovered from *T. cruzi* infection or which have been passively immunized by injection of immune rat serum. Partial and temporary immunity is passed to the young through the milk, but not to any effective extent through the placenta, and the intestine of the young is permeable to these immune bodies for about 20 days after birth. The immunity is specific.

MAZZA *et al.* (pp. 414, 415) have described the pathological appearances of the heart in Chagas's disease. MAZZA (p. 415) describes a condition of nodular hepatitis which he states to be of diagnostic importance in the post mortem examination of patients with Chagas's disease, and points out that specimens of liver and of heart may be taken with the viscerotome, which may thus be valuable in the study of the epidemiology of the disease.

ALBERTO AGUIRRE and GIMENEZ (p. 415) describe the changes in the heart found on X-ray examination in Chagas's disease. Enlargement of both ventricles is a marked feature and may occur in periodic fashion as if there were acute dilatation due to myopathy. Reduction in size takes place after treatment by rest and digitalis.

ROMAÑA (p. 416) describes in detail the histological pathology of the eye of a monkey infected by the deposition of infected faeces of *Rhodnius prolixus*.

LEITE (p. 416) records his opinion that the occurrence of goitre in patients suffering from American trypanosomiasis cannot be considered as an essential part of the picture of the disease.

MAZZA and his collaborators (p. 715) give clinical details of severe acute cases of Chagas's disease, in one of which there developed a rash, consisting of sharply defined red spots, on the body and legs.

Charles Wilcocks.

LEISHMANIASIS.

PRÉCIS OF ABSTRACTS IN THIS SECTION.

Visceral.

STEPHENSON (p. 250) reports a fatality rate of 80 per cent. in the recent epidemic of kala azar in the Dinka tribe of the Sudan. Even with standard treatment only a small proportion recovered. On the other hand MITRA (p. 251) reports that in 1937, 92,000 cases of kala azar

were treated in Bihar, and that treatment results in cure in 95 per cent. of cases. Intensive treatment is the only measure as yet possible in anti-kala azar campaigns. MAZZA (p. 251) discusses kala-azar in the Argentine.

HOEPPLI (p. 252) discusses the epidemiology of kala azar in China where *Phlebotomus chinensis* is readily infected from dogs. If in China canine kala azar is identical with the human infection, the dog must be regarded as the reservoir of the disease, as in the Mediterranean area. CHUNG (p. 252) goes further than this and remarks that there is considerable evidence that *L. donovani* and *L. canis* are identical and that in N. China the dog is the reservoir of the human disease. He records several findings in support of these views. YOUNG (p. 253) reports the formation of a granuloma in the leg of a hamster inoculated with a Chinese strain of *L. donovani*. It was formerly thought that such tumours were caused by *L. infantum* but not by *L. donovani*.

ISHII (p. 254) discusses the infection of laboratory animals, by different routes, by tissue forms and flagellates of leishmania.

HU (p. 254) shows that the chipmunk is susceptible to kala azar. ISHII *et al.* (p. 254) show that the Japanese striped squirrel is very susceptible to experimental intraperitoneal infection.

ADLER (p. 255) reports on an attempt to infect a patient (suffering from malignant disease) with *L. infantum* by injection. Leishmania in small numbers were found in the spleen at post mortem examination.

ADLER and ASHBEL (p. 255) describe the metabolism of tissues infected with leishmania. LIEU (p. 255) reports on the reactions of microglia cells in the brains of hamsters after intracerebral inoculation of leishmania.

HU (p. 256) discusses the influence of parenterally induced killed bacteria and foreign proteins on experimental kala azar infection in hamsters.

SMITH *et al.* (p. 256) report experiments on the transmission of kala azar by *P. argentipes* in India. They have succeeded in keeping sand-flies alive for long periods both before and after a feed of blood. They point out the importance of blocked flies in transmission. Of 13 animals (hamsters and mice) exposed to infection by *P. argentipes*, 7 became infected. Complete blocking of the flies is not essential but appears to produce particularly heavy infection.

GIRAUD and GAUBERT (p. 258) discuss the methods of diagnosis in kala azar, pointing out that in adults specimens from lymph glands cannot always be obtained. BENHAMON (p. 258) adds that skin scrapings are often helpful. ISHII *et al.* (p. 258) show that in the rabbit, inoculation of infected hamster liver results in heavy infection of the ciliary body. They suggest that this may be a useful diagnostic procedure. They report experiments with mice which clearly show that *L. donovani* is capable of passing through the placenta to the foetus.

LAHA (p. 259) points out that the aldehyde test usually only becomes positive 6 months after the onset of kala azar, and that in some cases it does not become positive even then. Other diseases may give confusing results. MARTINS (p. 259) has discussed the serological diagnosis of leishmaniasis.

GATTO (p. 259) considers that the anaemia of kala azar is not due to a haemolytic process, but to defects in blood production due to changes in the bone marrow.

ADAMS and YORKE (p. 260) report apparent cure in an Indian suffering from kala azar and treated with 4 : 4′-diamidino stilbene. KIRK and SATI (p. 260) report on the treatment of kala azar with 4 : 4′-diamidino stilbene. The results are apparently favourable though the details of dosage have not yet been fully worked out. Toxic symptoms are negligible. KIRK and MACDONALD (p. 261) report a case from the Sudan in which visceral, cutaneous and mucosal leishmaniasis were present; treatment with 4 : 4′-diamidino diphenoxy pentane was apparently successful.

KIRK and SATI (p. 261) describe a punctate rash which occurs in about 20 per cent. of patients who are responding well to treatment with neostibosan. It is usually seen on the face, there is no tendency to ulceration and there are no subjective symptoms. The eruption tends to disappear spontaneously. The rash may be due to aggravation of skin lesions during treatment and may be analogous to the Herxheimer reaction in syphilis [in which symptoms are increased after the administration of a small dose of salvarsan or mercury.]

WANG (p. 262) has examined the spleens of infected hamsters at different periods during treatment with neostibosan; there are three stages, one of proliferation of plasma cells and lymphocytes, one of degeneration of the host cells and disappearance of the parasites, and finally one of repair. All the important changes are observed during the first three weeks.

Cutaneous and Muco-cutaneous.

HALAWANI (p. 263) discusses the distribution of oriental sore in Egypt. MARCHIONINI (p. 263) discusses the clinical features of oriental sore in Turkey.

AKAN (p. 263) states that oriental sore has been successfully treated with atebrin.

PESSÔA *et al.* (p. 264) discuss the epidemiology of muco-cutaneous leishmaniasis in São Paulo, which, even in the areas of high endemicity, is largely a rural disease.

GEIMAN (p. 264) has studied *L. brasiliensis*, and finds that whereas *L. tropica* easily infects the chorio-allantoic fluid of the developing fowl embryo, and remains actively motile and can be passaged at least 26 times, *L. brasiliensis* becomes non-motile and only survives to the second passage. *C. W.*

STEPHENSON (R. W.). **An Epidemic of Kala-Azar in the Upper Nile Province of the Anglo-Egyptian Sudan.**—*Ann. Trop. Med. & Parasit.* 1940. Sept. 26. Vol. 34. No. 2. pp. 175–179. With 1 map.

In the Sudan the main endemic centre of the disease appears to be along the Abyssinian border, from which extensions occur along the rivers. In recent years, however, sporadic cases have been found over the whole country, so that it seems probable that few areas are free from it. The present paper describes an epidemic which occurred among a small section of the Dinka tribe in an area west of the White Nile and some hundred miles north of Malakal. The epidemic commenced in 1932 and lasted for about 8 years. It is estimated that amongst a population of 8,000 people during the space of three years there must have been at least 300 cases, with a fatality rate of 80 per

cent. About 30 miles to the east of the area is a district inhabited by a tribe called the Maaban, amongst whom, at the Jongols Post, ARCHIBALD in 1923 described an outbreak amongst the troops [this *Bulletin*, 1923, Vol. 20, p. 867]. In recent years there has been contact between the Maaban and Dinkas and it would seem that this has been the cause of the outbreak described in this paper. The disease during the epidemic was of an acute type and of cases admitted to hospital and given standard treatment only a low percentage recovered. Evidence was obtained that cases with cancrum oris had a better chance of recovery when treated with ureastibamine. *C. M. Wenyon.*

BIHAR, PROVINCE OF: ANNUAL PUBLIC HEALTH REPORT FOR YEAR 1938 AND ANNUAL VACCINATION REPORT FOR YEAR 1938–39 [MITRA (S. L.), Director]. [**Kala Azar** p. 18.]

"*Kala-Azar.*—A report on Kala-Azar in Bihar by the Inspector-General of Civil Hospitals brought to light in December 1938 even more prominently than was known so far that the Kala-Azar situation in North Bihar is acute. A total of 92,000 cases of Kala-Azar were treated in the hospitals and dispensaries of Bihar in 1937 and of them 83,961 cases were treated in the districts of North Bihar. . . .

"A thorough treatment brings about 95 per cent. cure in Kala-Azar cases whilst it is difficult to formulate preventive measures in the absence of knowledge of the exact means of the spread of the disease. An anti-Kala-Azar campaign has, therefore, to be restricted to the provision of intensive treatment in the affected areas. With a view to launching an intensive campaign in Bihar, Government sanctioned the scheme for establishing 15 additional centres in North Bihar, viz., six in Purnea, three each in the districts of Muzaffarpur, Darbhanga and Bhagalpur and one in Chota Nagpur, viz., Hazaribagh, during 1939–40."

MAZZA (Salvador). El kala-azar en la República Argentina. [**Kala Azar in the Argentine.**]—Reprinted from *Las Actas y Trabajos del VI Congreso Nacional de Medicina, Cordoba.* 1939. Vol. 3. 8 pp.

The author notes that the first autochthonous case of kala azar was one described by himself in 1926. It had been diagnosed by spleen puncture and the discovery of leishmania. In 1932 two further cases were seen. These were diagnosed on clinical grounds alone but there was no doubt as to the correctness of this diagnosis. In 1936 two other cases came to light, but the author had some difficulty in obtaining the spleen smears from the medical men in attendance. However, when these were procured leishmania were demonstrated in both. Later, one of the medical men, a former member of M.E.P.R.A. (the mission studying regional pathology in the Argentine), became a member of a commission from the Oswaldo Cruz Institute to study the distribution of kala azar in S. America and he is stated to have given the commission incorrect information about the two cases of kala azar seen by him in the northern Argentine. [The paper is a controversial one and rather suggests that the medical man in question was ill advised to desert the Argentine mission for that of Brazil.]

C. M. W.

HOEPPLI (R.). **The Epidemiology of Kala-Azar in China.**—*Chinese Med. Jl.* 1940. Apr. Vol. 57. No. 4. pp. 364–372. [40 refs.]

In discussing the epidemiology of kala azar in China the author notes that though sporadic cases have been reported from West, Central and South China, the real home of the disease is north of the Yangtse Valley. Investigations have shown that the parasite develops in the sandfly, *Phlebotomus chinensis*, which readily becomes infected when fed on experimentally infected hamsters and less readily when fed on human beings, the difference being due to the presence of fewer leishmania in the skin of man. Canine kala azar is common in Peiping and sandflies are readily infected when fed on dogs suffering from the disease. If it can be established that the canine disease in North China is identical with the human kala azar of that region, then the dog will have to be regarded as a reservoir of the human disease, as it is in the Mediterranean foci. The fact that leishmania may be found in the nasal secretion, urine or faeces of kala azar cases does not appear to throw any light on the spread of the disease, any more than the discovery of malarial parasites in blood escaping from the nose or intestine would have any bearing on the epidemiology of malaria.

C. M. W.

CHUNG (Hui-Lan). **On the Relationship between Canine and Human Kala-Azar in Peiping and the Identity of** *Leishmania canis* **and** *Leishmania donovani*.—*Chinese Med. Jl.* 1940. June. Vol. 57. No. 6. pp. 501–522. With 1 text fig. & 12 figs. on 4 plates. [44 refs.]

The study of human and canine kala azar, both in the field in and around Peiping and in the laboratory, has brought increasing evidence of the identity of the human *Leishmania donovani* and the so-called *L. canis* of dogs. At the same time it has given support to the view that the dog in N. China, as in the Mediterranean region, is the reservoir from which human cases derive their infection. Much of the evidence has been described in earlier papers but in the present one a number of new and interesting observations are recorded. It is shown that there is in Peiping city itself a very close association between cases of kala azar in dogs and cases in human beings, an association which is clearly indicated in a very instructive spot map. It is shown that in a small village seven miles from Peiping the identification and treatment of all cases of kala azar was not followed by the disappearance of the disease, as might have been expected if there was only human case to case infection. Subsequent observations showed that the dogs of the village suffered from the disease and appeared to have been acting as a reservoir from which the infection spread to human beings. Negotiation for the control of the dogs is in progress and it is hoped that by this means the disease will be eradicated. Evidence has been produced in the laboratory to show that hamsters cured of one infection show some degree of immunity to the other, while a young man who had been cured of kala azar has so far not shown any signs of infection following inoculation with flagellate forms of the canine leishmania. Complement fixation tests carried out with antigens prepared from both strains of parasite failed to reveal any differences between the two. The parasites are not only morphologically identical but they are also indistinguishable as regards pathogenicity and histopathological reactions in experimental animals—dogs, hamsters, moles and chipmunks. As in the

Mediterranean region, the canine disease is marked by heavy leishmanial infections of the skin, a fact which enables sandflies to be much more readily infected from dogs than from human beings. The infections produced in hamsters by the human and canine strains of parasite are identical and, in conformity with this, *Phlebotomus chinensis* is as readily infected by feeding on hamsters harbouring the one strain as on those harbouring the other. Similarly *P. chinensis* becomes easily and heavily infected with either strain, while *P. sergenti* var. *mongolensis* is less readily infected. In the case of *P. chinensis* migration of flagellates forwards to the pharynx and proboscis is of common occurrence, while with *P. sergenti* the infection is less intense and seems to persist only if blood is present in the stomach. From the arguments brought forward in the paper and outlined above it appears impossible to hold any other view than that the two strains are identical. Nevertheless, as a final test, a volunteer has allowed himself to be inoculated with the canine strain. Though the final result has not yet been obtained, certain haematological and serological changes have occurred which are in favour of infection having taken place. In an appendix to the paper a series of case reports is given, illustrating the association of the human with the canine disease, while in a number of photographs are shown the cutaneous lesions in infected dogs and the appearance of sections of the skin and internal organs heavily infected with leishmania. *C. M. W.*

YOUNG (Shutsu). **A Granuloma of the Foreleg of a Hamster** *Cricetulus griseus* **artificially infected with Chinese Kala-Azar.**—Reprinted from *Jl. Shanghai Sci. Inst.* 1940. Apr. Sect. 4. Vol. 5. pp. 125–132. With 13 figs. on 4 plates. [13 refs.]

The author gives an account of a Chinese hamster which was inoculated with a Chinese strain of *Leishmania donovani*. The animal acquired a generalized infection, parasites being discovered in macrophages, in the skin and all the organs examined post mortem one year after the inoculation. About three months before its death the hamster developed a tumour-like swelling of the left foreleg which was adherent to the periosteum. On section the nodule, which was in the form of two lobes, was found to consist of macrophages and fibroblasts. The former were filled with leishmania, while the latter also contained these parasites in varying number. The deeper fibroblasts contained many collagen fibrils and no parasites, while the superficial fibroblasts formed fewer fibrils and contained a number of parasites. The origin of the macrophages in the nodule is discussed and though it is admitted that some may have originated from the macrophages or clasmatocytes normally present in the skin it is concluded that some may have originated from the spindle-shaped fibroblasts. Though similar tumours on the legs of animals inoculated with other strains of kala azar leishmania (*Leishmania infantum*) have been reported, this is the first time that such a lesion has resulted from infection with a Chinese strain. The interest of the observation lies in the fact that at one time the failure to produce such tumours in animals infected with the Chinese strain of leishmania of kala azar was regarded as a character distinguishing it from *Leishmania infantum*, which was known to cause lesions of the kind. *C. M. W.*

ISHII (Nobutaro). **Studies on Kala-Azar. (Report I.) (I.) Experimental Studies on Infection Routes. (II.) Transmission Experiments on Several Animals.**—*Japanese Jl. Experim. Med.* 1940. June 20. Vol. 18. No. 3. pp. 137–146. [32 refs.]

The author, working in Japan, has shown how laboratory animals may be infected with leishmania by a number of different channels. Oral administration of liver emulsion of heavily infected hamsters has produced a generalized infection in eight hamsters. Application of emulsion to the abdominal wall of hamsters, after removal of the hairs by clipping with scissors so as not to injure the skin in any way, led to infection in four out of nine animals. The flagellate culture forms were unable to traverse the skin. Intracerebral inoculation of emulsion of infected liver into hamsters led to cerebral infections. Flagellate forms of *L. donovani* and *L. tropica* were unable to cause infections of the brain in this way. Inoculation of white mice intracerebrally with liver emulsion containing *L. donovani* or with the culture form of this organism and *L. tropica* led to infection of the brain in a number of instances. It was found that inoculation of cultural forms intraperitoneally to mice did not give rise to infection unless the peritoneal cavity had previously been injected with snake venom, iron sugar solution, starch or liver suspension. Inoculation of infective liver suspension into the anterior chamber of the rabbit's eye resulted in infection of the cilia and cornea two to four weeks later. It is noted that the Japanese striped squirrel (*Eutamias asiaticus*) is as susceptible to *Leishmania donovani* as is the Chinese hamster. *C. M. W.*

HU (C. H.). **The Susceptibility of Normal and Sarcosporidia Infected Chipmunks** (*Eutamias asiaticus senescens*) **to Kala Azar.**—*Chinese Med. Jl.* 1940. Mar. Supp. 3. pp. 192–194. With 6 figs. on 3 plates.

The paper records the fact that the chipmunk (*Eutamias asiaticus senescens*), a squirrel-like striped animal of 100 to 120 gm. weight, is susceptible to infection with kala azar. The generalized infections produced are similar to those so readily obtained in hamsters. As these animals are larger and more easily handled than Chinese hamsters they are likely to be useful animals for certain types of experimental work.

C. M. W.

ISHII (Nobutaro), SAWADA (Toshisada) & SHIMIZU (Shigeya). **Studies on Kala-Azar. (Report II.) On the Susceptibility of the Japanese Striped Squirrel.**—*Japanese Jl. Experim. Med.* 1940. June 20. Vol. 18. No. 3. pp. 147–156. With 13 figs. on 2 plates.

In this paper a detailed account is given of a large series of inoculation experiments carried out with *Leishmania donovani* and Japanese striped squirrels. Heavy infections result within two months of intraperitoneal inoculation of emulsion of infected liver. Practically every organ of the body becomes infected, the changes in the organs and the intensity of the infections being similar to those produced by the inoculation of Chinese hamsters. The infection rate following inoculation is as much as 100 per cent. *C. M. W.*

ADLER (S.). **Experimental Visceral Leishmaniasis in Man.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1940. Nov. 30. Vol. 34. No. 3. pp. 293–294.

In a previous paper [this *Bulletin*, 1940, Vol. 37, p. 768] the author has shown that the repeated injection of large doses of the cultural forms of the leishmania of kala azar into five patients debilitated from inoperable cancer produced infection in only one instance. It was suggested that the lytic action of normal human serum on flagellate forms of leishmania might account for the difficulties of infection, as the parasites would be liable to destruction before they were established in the reticulum cells. That some other factors are involved is indicated by the fact that rabbits are difficult to infect with leishmania, though their blood is far less lytic than that of human beings.

In the present paper an account is given of a further attempt to infect a patient suffering from carcinoma. Leishmania from the spleen of a Syrian hamster infected with *Leishmania infantum* were injected intragluteally, while a month later another similar injection was given into enlarged supraclavicular glands. Seventeen days after the last injection the patient died. At post mortem examination leishmania were found only in small numbers in the spleen. It was noted that the serum of this patient, who was jaundiced, was not lytic to the cultural forms of leishmania, a fact which may have accounted for the infection, which resulted from the relatively small doses of the parasite injected.

C. M. W.

ADLER (S.) & ASHBEL (Rivkah). **A Note on the Metabolism of Tissues infected with** *Leishmania donovani, L. infantum* **and** *L. tropica.*—*Ann. Trop. Med. & Parasit.* 1940. Dec. 31. Vol. 34. Nos. 3 & 4. pp. 207–210.

The authors have shown that slices of liver and spleen of animals infected with leishmania, when tested in a Barcroft-Warburg apparatus, produce aerobic glycolysis in contrast to uninfected tissues, which do not. The oxygen consumption of infected tissues is also greater than that of normal tissues. Individual infected cells act in the same manner. On the other hand suspensions of leishmania freed from tissue by a process of centrifugation produce no appreciable aerobic glycolysis. In this respect the leishmania stage of the parasite differs from the flagellate stage. *C. M. W.*

LIEU (V. T.). **Experimental Cerebral Leishmaniasis (Kala-Azar) in Hamster with Special Reference to the Reaction of Microglia toward the Parasite.**—*Chinese Med. Jl.* 1940. Mar. Supp. 3. pp. 186–191. With 8 figs. on 2 plates. [15 refs.]

By injecting suspensions of leishmania obtained from the spleens of heavily infected hamsters into the cerebral hemispheres of hamsters and examining the brains from one to 37 days later, it was found that the leishmania were phagocyted by round modified microglia cells. The amoeboid microglia cells occasionally contained parasites but the normal microglia and faintly staining astrocytes never did. The parasites were located at the site of injection and were never found elsewhere in the brain. *C. M. W.*

HU (C. H.). **The Influence of Parenterally Introduced Killed Bacteria and Foreign Proteins on Experimental Kala-Azar Infection in Hamsters.**—*Chinese Med. Jl.* 1940. Mar. Supp. 3. pp. 179–185. With 6 figs. on 3 plates.

Owing to the fact that certain intercurrent infections in kala azar, such as pneumonia and cancrum oris, may be followed by complete disappearance of leishmania from the body, experiments were instituted to test the influence of repeated intraperitoneal injections of bacteria, horse serum or beef broth on a kala azar infection in hamsters. It was found, after weekly injections over a period of two months, that in no case was leishmania infection prevented, though, from the feebleness of the infection in some cases, it appeared that some degree of resistance had been conferred. It was noted that two types of spleen enlargement occurred. In one the greatly enlarged organ contained scattered nodules composed of reticulo-endothelial cells in which relatively few leishmania occurred. In the other case the spleen was less enlarged, while the reticulo-endothelial proliferation was less active. The cells, however, were not collected to form nodules but were more or less uniformly scattered through the organ. In this case the cells were loaded with parasites. *C. M. W.*

SMITH (R. O. A.), HALDER (K. C.) & AHMED (I.). **Further Investigations on the Transmission of Kala-Azar. Part I. The Maintenance of Sandflies** *P. argentipes* **on Nutriment other than Blood.**—*Indian Jl. Med. Res.* 1940. Oct. Vol. 28. No. 2. pp. 575–579. **Part II. The Phenomenon of the 'Blocked' Sandfly.**—*Ibid.* pp. 581–584. **Part III. The Transmission of Kala-Azar by the Bite of the Sandfly** *P. argentipes.*—*Ibid.* pp. 585–591.

In this series of papers the authors give an account of further experiments which go far to establish beyond doubt the responsibility of *Phlebotomus argentipes* in the transmission of kala azar in India.

In the first it is shown how it has been found possible to keep sandflies alive for long periods, both before and after a feed of blood, by allowing them to nourish themselves on raisins. Thus, of 1,566 flies which had a blood meal and were subsequently fed on raisins 855 were alive on the tenth day. After the digestion of the blood meal on the third day the flies are introduced into a glass lamp chimney of about 700 cc. capacity, where they have access to moistened cotton wool and raisins. Eggs are deposited on the moist wool. After oviposition has once taken place no more egg laying occurs owing to absence of further blood meals. Apart from the longer survival of the flies there is the added advantage from the point of view of transmission experiments that the development of leishmania is not interrupted in any way—on the contrary, a larger proportion of flies is found with a heavier infection. This observation has shown that the previous assumption that blood feeds would be necessary for the satisfactory development of leishmania in the flies was erroneous. Whether in nature the flies survive on fruit juices with occasional feeds of blood has not yet been determined, but there is evidence that they resort to vegetation.

In the second paper the development of leishmania in flies kept under the new conditions is discussed, particularly with reference to the phenomenon of blocking first noted in 1926 by SHORTT, BARRAUD and CRAIGHEAD, who compared it with the blocking of the oesophagus

of fleas with plague bacilli [this *Bulletin*, 1927, Vol. 24, p. 132]. As with blocked fleas, the flies in this condition are unable to ingest blood, though they make strenuous efforts to do so. It thus comes about that it is possible to identify the blocked flies during life owing to this failure to imbibe blood after attempting to feed on an experimental animal. Of 225 known positive flies dissected, 58 had been diagnosed as blocked, and of these 49 at least were shown by dissection to be heavily infected with flagellates. Such blocked flies do not live longer than one or two days, so that for purposes of transmission experiments it was necessary to isolate them as soon as recognized. As a rule the flies, after a first feed on a kala azar patient, are kept on a diet of raisins till the tenth day before being offered a second blood meal on an experimental animal. Flies which succeed in ingesting blood, and which are therefore not blocked, were separated and kept for future blood feeds, but in no case were blocked flies found amongst these when offered a third or fourth blood meal. Blocked flies are thus found only amongst those attempting to feed on blood a second time. It is assumed that the vain attempts made by the blocked flies to suck blood result in flagellates being dislodged and discharged into the proboscis wound in the skin.

The third paper describes the actual transmission experiments. It is recalled that the first successful transmission of *Leishmania donovani* by the bite of the sandfly *P. argentipes* was obtained in a hamster in 1931 by SHORTT, SMITH, SWAMINATH and KRISHNAN [this *Bulletin*, 1932, Vol. 29, p. 107]. It was one of two which had survived 17 months after the beginning of the experiment. In 1933, NAPIER, SMITH and KRISHNAN infected two out of 28 animals, while in 1935, SMITH, LAL, MUKERJEE and HALDER succeeded with one out of 16. These results, though confirming the view that *P. argentipes* was capable of transmitting kala azar, were not quite those which would be expected in experiments on the very susceptible hamsters if *P. argentipes* was the real vector. The new facts noted above appearing to offer better opportunities of transmission, further experiments with the new technique were instituted. Flies, after a preliminary feed on a kala azar patient, were maintained till the tenth day on a diet of raisins and then offered a second blood meal on an experimental animal. Five hamsters and ten mice were exposed to the bites of such flies but two mice died shortly after, thus leaving in all 13 animals. Of these seven, two of which were mice, have been proved to have become infected. The longest period which elapsed before infection was determined was seven months in the case of one mouse. It has become evident that complete blocking is not necessary for transmission, for the two mice infected had not been bitten by completely blocked flies. On the other hand, one hamster upon which blocked flies alone had fed had a particularly heavy infection. Though it seems reasonable to suppose that the success of these experiments was dependent upon the inoculation of heavy doses of flagellates by blocked or partially blocked flies, it still has to be remembered that there may have been an increase in virulence of the leishmania during its development in the flies fed on the raisins. So far no evidence in favour of such an increase in virulence has been obtained. It is known, however, that human blood serum has a lytic effect on the flagellates, a fact which may account for the less intense infections in flies kept alive on blood instead of on raisins, as in the experiments just described. Whether the continued blood feeding brings about also a decrease in virulence is not

known. Whatever may be the explanation of the success of the experiments, the results are those which were to be expected of the sandfly *P. argentipes* since it was discovered epidemiologically to be so closely connected with the spread of kala azar.

Though the authors speak of the final test of transmission to human beings, there can hardly remain, after the experiments they have described, any vestige of doubt that *L. donovani* in India is transmitted by *P. argentipes* and that sandflies in general are vectors of leishmania throughout the world. *C. M. W.*

i. GIRAUD (P.) & GAUBERT. Valeur pratique des divers procédés de recherche des leishmanies pour le diagnostic du kala-azar méditerranéen. [**Practical Value of Various Methods of detecting Leishmania for the Diagnosis of Mediterranean Kala-Azar.**]—*Presse Méd.* 1938. Vol. 46. pp. 4–6.

ii. BENHAMON (E.). La recherche des leishmanies dans le diagnostic du kala-azar. [**The Search for Leishmanial Bodies in the Diagnosis of Kala-Azar.**]—*Ibid.* pp. 121–122. With 6 figs. [Numerous refs.] [Summary taken from *Vet. Bull.* 1940. Nov. Vol. 10. No. 11. pp. 831–832. Signed U. F. RICHARDSON.]

i. Discussing the diagnosis of human leishmaniasis, the authors state that serological tests are not absolutely reliable, and that the presence of the parasites should always be demonstrated. The examination of the blood, liver and skin, and attempts to culture from blood or spleen all gave unsatisfactory results. Spleen puncture gave the best results, but is said to cause a mortality of 1 per cent. from internal haemorrhage. Examination of bone marrow, obtained in adults from the sternum and in children by trephining the tibia near the epiphysis gave very reliable results, and it is said to be simple, not painful, and free from danger. In children the puncture of lymph nodes gave results almost as reliable as those obtained by spleen puncture, but in adults lymph node specimens could not always be obtained.

ii. Benhamon recommends sternal puncture with a trocar needle as the method of choice for routine examination for leishmanial infection. It only requires simple aseptic precautions, is reliable, free from danger to the patient and does not necessitate rest in bed. He points out that monocytosis of the lymph node juice is almost diagnostic of leishmaniasis, apart from the presence of leishmanial bodies. He agrees with GIRAUD and GAUBERT (see i) as to the value of other methods of detecting infection, except that he considers that skin scrapings are often an aid to diagnosis. He points out that, in fact, all the methods have their uses in diagnosis and in estimating the severity of infection.

ISHII (Nobutaro), SAWADA (Toshisada) & SHIMIZU (Shigeya). **Studies on Kala-Azar. (Report III.) (I.) Inoculation Experiment into the Fore-Chamber of the Rabbit Eye. (II.) Experimental Study on Prenatal Infection.**—*Japanese Jl. Experim. Med.* 1940. June 20. Vol. 18. No. 3. pp. 157–163. With 4 figs. on 1 plate.

In this paper further details are given of the effect of inoculating leishmania into the anterior chamber of the rabbit's eye. Inoculation of emulsion of infected hamster liver resulted in heavy infection, chiefly of the corpus ciliare. This reached its greatest intensity two to

four weeks after inoculation. It is suggested that this response might be employed for diagnostic purposes. Similar inoculation of the flagellate stages of *L. donovani* and *L. tropica* produced slight infections.

Experiments were carried out to test the possibility of placental infection. A female mouse gave birth to four offspring 74 days after she had been infected with *L. donovani*. Three days later the four young were placed in the care of another female which was feeding five of her own. At the same time the five young were transferred to the infected mother. Later the young mice were examined and one of the young born of the infected mother was found infected. Not one of the five which had been nourished on the milk of the infected female had become infected. Further observation showed that three young of an infected mother, which were examined the day after their birth, were not infected. Four similarly born and examined seven days after birth showed that two were infected, while not one of three, also born of an infected female, was found infected when examined on the 59th day. It is thus clear that *L. donovani* is capable of passing through the placenta to the foetus. *C. M. W.*

LAHA (P. N.). **Limitations of the Aldehyde Test in the Diagnosis of Kala-Azar.**—*Jl. Indian Med. Assoc.* 1940. June. Vol. 9. No. 9. pp. 427–428.

The author notes that though the aldehyde test for kala azar is the one most frequently employed in the diagnosis of the disease it has to be remembered that the changes in the blood which are responsible for it are of slow development. Rarely is a positive result obtained before the disease has lasted for four months, while usually a period of six months is required. Certain other diseases, such as advanced tuberculosis, leprosy, schistosomiasis or trypanosomiasis, may give confusing results. A case of malaria in a boy of 14 is mentioned; his serum gave a positive aldehyde test. Kala azar was suspected and a spleen puncture performed. In place of the expected leishmania, malignant malarial parasites were found. Seven cases of kala azar in patients from 12 to 30 years of age, in which the disease was over six months in duration, are mentioned on account of the failure of the serum to give a positive aldehyde test. *C. M. W.*

MARTINS (A. Frância). Do diagnóstico sorologico das leishmanioses. [**Serological Diagnosis of Leishmaniasis.**]—*Ann. Paulist. Med. e Cirurg.* 1940. Apr. Vol. 39. No. 4. pp. 251–264. [24 refs.]

The article, which does not contain any new observations, is a general account of the various serological reactions which have been employed in the diagnosis of leishmaniasis. It is intended, no doubt, for the guidance of medical men in S. America who may come across suspected cases of kala azar, endemic foci of which have comparatively recently been brought to light. *C. M. W.*

GATTO (Ignazio). Ricerche sul ricambio emoglobinico nella leishmaniosi viscerale. [**Haemoglobin Variation in Visceral Leishmaniasis.**]—*Settimana Med.* Palermo (formerly *Riv. Sanitaria Siciliana*). 1940. Feb. 9. Vol. 28. No. 6. pp. 142, 145–8. [30 refs.]

An investigation of eight cases of infantile kala azar has shown that the degree of bilirubinaemia and the haemolytic index were in seven

of the cases within the normal limits, both at the commencement and at the completion of a course of antimony treatment. The conclusion can be drawn that the anaemia of kala azar is not due to an increase in the haemolytic process but to defects in blood production due to changes in the bone marrow. *C. M. W.*

ADAMS (A. R. D.) & YORKE (Warrington). **Studies in Chemotherapy. XXV.—A Second Case of Indian Kala-Azar treated with 4 : 4′-Diamidino Stilbene.**—*Ann. Trop. Med. & Parasit.* 1940. Sept. 26. Vol. 34. No. 2. pp. 173–174.

In a previous paper [this *Bulletin*, 1940, Vol. 37, p. 775] the authors have described the successful treatment of a case of kala azar with the drug. The present paper gives an account of the treatment of a second case in a Hindoo seaman, aged 26, from Calcutta. The drug was given intravenously each day for 8 days in a dose of about 1 mgm. per kilo. of body-weight, the total amount administered being 400 mgm. The only immediate effect was an increase in the daily excursions of the temperature, which fluctuated between the normal and 104°F. After 4 days the temperature fell, till on the 7th day it remained at normal. The spleen, which was enlarged to below the umbilicus, quickly became reduced in size. The patient left hospital 6 weeks after the commencement of treatment apparently cured, attempts to discover parasites by spleen and sternal puncture ten days before his discharge having failed. *C. M. W.*

KIRK (R.) & SATI (Mohammed Hamad). **Notes on Some Cases of Sudan Kala-Azar treated with 4 : 4′-Diamidino Stilbene.**—*Ann. Trop. Med. & Parasit.* 1940. Sept. 26. Vol. 34. No. 2. pp. 83–92. [10 refs.]

In this paper the authors describe the treatment of a number of cases of kala azar in the Sudan with diamidino stilbene. Eight of these are considered in detail, the case histories being given. There were two deaths, in patients who were moribund when treatment was commenced, and six recoveries in cases which have shown no signs of relapse during four months' observation. Twenty other cases have also been treated with the drug but the length of control has been short. Of these, two have died, three were still in hospital when the paper was written, while the remainder had been discharged as apparently cured. The total dosage of the drug to bring about cure varies from case to case. Thus, one case was cured by 975 mgm. given in 24 injections during a period of five weeks, while another required 4·4 gm. given in 70 injections during six months. It was thought that the daily dose was more effective than dosage on alternate days. The standard solution for intravenous injection was made by dissolving 100 mgm. in 10 cc. of distilled water. It is admitted that the best scheme of treatment has yet to be worked out, but it is already evident that, just as is the case with antimony treatment, there is marked individual variation as regards the quantity of drug required to bring about a cure. In the doses used, 1 to 2·6 mgm. per kilo. of bodyweight, toxic symptoms were negligible, but it was noted that at the commencement of a course of treatment there was not infrequently an exacerbation of the signs and symptoms of the disease. As occurs sometimes during antimony treatment, punctate and nodular skin

lesions, in which leishmania may be found, are apt to appear during a course of diamidino stilbene. In assessing the results of treatment no opinion is expressed as to whether these are better than those which would be expected from antimony treatment. It is noted that the Sudan cases are notoriously difficult to treat, owing to the frequent occurrence of such complications as intractable diarrhoea, haemorrhages, cancrum oris and lobar pneumonia, quite apart from concomitant infections, of which helminthiasis, malaria, amoebic and bacillary dysentery are the commonest. *C. M. W.*

KIRK (R.) & MACDONALD (D. R.). **An Unusual Case of Leishmaniasis treated with 4 : 4′-Diamidino Diphenoxy Pentane.**—*Ann. Trop. Med. & Parasit.* 1940. Sept. 26. Vol. 34. No. 2. pp. 131–134. With 2 figs. on 1 plate.

A young native in the Sudan, 24 years of age, was treated for kala azar with neostibosan. Response was more rapid than is usual with cases of this disease in the Sudan, so that the patient was discharged as cured from the Omdurman hospital on the 45th day of observation. He returned 13 days later suffering from bilateral anterior tibial paralysis with double foot-drop. There was a very conspicuous nodular depigmented eruption on the face and a minutely punctate rash over the remainder of the body. Rhinoscopy revealed a large flat ulcer on the nasal septum. Smears from the ulcer and a nodule on the face revealed leishmania. There was no fever and the patient felt quite well. The spleen was still palpable. After 49 days' rest in hospital, during which the neuritis disappeared, treatment with the drug named in the title of the paper was commenced. It was administered intravenously on alternate days in 10 cc. of distilled water. Ten doses of 80 mgm. and 13 doses of 100 mgm. were given, a total of 2·1 gm. There were no toxic symptoms. The spleen decreased in size and the cutaneous and nasal lesions subsided. A month after discharge from hospital the patient was again seen, when the spleen was no longer palpable. Smears from the skin and inside of the nose failed to reveal leishmania.

Discussing the case, the authors note the resemblance of the cutaneous eruption after successful treatment of a visceral infection to post kala azar dermal leishmaniasis of India. The rapid disappearance of the skin lesions after the treatment is, however, a point of difference. The nasal mucosal lesion suggests espundia, cases of which have been recorded for the Sudan. The case described is the first in which visceral, cutaneous and mucosal leishmaniasis have been found in one individual. *C. M. W.*

KIRK (R.) & SATI (Mohammed Hamad). **Studies in Leishmaniasis in the Anglo-Egyptian Sudan. IV. A Punctate Rash in Treated Cases.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1940. Aug. 16. Vol. 34. No. 2. pp. 213–216. With 4 figs. on 1 plate.

In an earlier publication from the Sudan KIRK and DREW [this *Bulletin*, 1938, Vol. 35, p. 877] mentioned a finely punctate eruption which appeared during the course of antimony treatment of cases of kala azar in that country. In the present paper a fuller account of this rash is given. It occurs in about 20 per cent. of cases, usually after the first or during a second course of treatment, when fifteen to thirty

doses of neostibosan have been given. It appears only in cases which are reacting favourably to the treatment and is thus of some prognostic significance. It is first seen on the face, on the forehead or malar region as a minute punctate rash. It may be restricted to these regions but more usually the whole face and neck become involved. In the coarser forms the puncta are readily palpable and might be described as papules. In some cases sudamina accompany the rash, while in others the individual puncta are difficult to distinguish, there being an appearance of xerodermia or mild ichthyosis. Rarely the rash extends to other parts of the body. There is no tendency to ulceration and subjective symptoms are lacking. Unlike the post kala azar dermal leishmaniasis of India, which usually appears a year or more after treatment is completed, the eruption under discussion tends to disappear spontaneously within a few months after discharge from hospital. The view that the rash is the direct result of the antimony is disproved by the observation that it may occur during treatment with 4 : 4′-diamidino stilbene. Careful examination has shown the presence of leishmania in small numbers in scrapings from the papules, but as these parasites may also be demonstrated in scrapings of apparently healthy skin of patients who have had no treatment their presence in the lesions has little significance. It has been noted by AUGIER and FAURE-BRAC [this *Bulletin*, 1935, Vol. 32, p. 490] that the cutaneous lesions which commonly occur in dogs suffering from kala azar become aggravated during antimony treatment and they consider this phenomenon to be analogous to the Herxheimer reaction. It may be that the appearance of the eruption in the Sudan cases of kala azar has a similar explanation. *C. M. W.*

WANG (C. W.). **A Histopathological Study of the Spleen of Kala-Azar Hamsters undergoing Treatment with Neostibosan.**—*Chinese Med. Jl.* 1940. Mar. Supp. 3. pp. 564–573. With 14 figs. on 7 plates.

A series of hamsters was infected by intraperitoneal inoculation of spleen emulsion of an infected hamster. Three months later, by biopsy, a portion of spleen of all the animals was removed for study by smear and section. Fourteen to 18 days later the surviving hamsters were given neostibosan treatment in doses of 400 mgm. per kilo. of body weight administered subcutaneously three times a week till a total of 15 gm. per kilo. had been given. From time to time pairs of hamsters were killed and the spleens removed for smear and section preparations. All the hamsters which survived the operation remained in apparently good health in spite of their infections and treatment. The spleen showed definite decrease in size from the thirteenth day onwards. Histopathologically the changes in the spleen during treatment of 32 hamsters may be divided into three stages. The first is characterized by the proliferation of plasma cells and lymphocytes. As at this stage there is no reduction in the number and size of the parasite-containing cells, the spleen is presumably increased in size. In the second stage, one of resolution, there is degeneration of the host cells and disappearance of the parasites. During this process the parasites seem to disappear before the degeneration of the host cells, the cytoplasm of which seems to degenerate first. It appears likely that under treatment the cytoplasm of the reticulo-endothelial cells no longer serves as a favourable medium for the

survival of parasites. The degeneration of the cells follows one of two courses. They degenerate and disintegrate, or they contract in size and become atrophic. There is no evidence of phagocytosis. The third and final stage is that of repair, the end result following one or other of the following lines: (1) lymphocytic hyperplasia, (2) thickening of trabeculae, (3) return to normal architecture, (4) fibroplastic proliferation. Though hamsters were examined up to 88 days after treatment had commenced, all the more important and characteristic changes were observed during the first three weeks.

C. M. W.

HALAWANI (A.). **On the Distribution of Oriental Sore in Egypt.**—*Jl. Egyptian Med. Assoc.* 1940. Apr. Vol. 23. No. 4. pp. 192–198. With 2 figs.

The author traces the development in knowledge regarding the occurrence of oriental sore in Egypt up to the discovery by KHALIL Bey in 1933 of an endemic focus at Hehia to the East of the Nile Delta near the town of Zagazig. The examination of suspected cases in the Skin Department of the Kasr El Aini hospital in Cairo has shown that other endemic foci probably exist. Cases positive for *Leishmania tropica* were from the following localities: Souhag and the neighbouring village of El Battack; Tal El Zaka, Markaz Tema; Beni Mohamed, Markaz Abnoub, Assiut Province; Rosetta; Imam El Shafei, Cairo.

C. M. W.

MARCHIONINI (Alfred). Zur Klinik der Hautleishmaniose: Typische und atypische Erscheinungsformen. [**Typical and Atypical Forms of Oriental Sore.**]—*Türkische Ztschr. f. Hyg. u. Experim. Biol.* Ankara. 1940. Vol. 2. No. 1. pp. 45–57. With 12 figs. [Turkish version pp. 39–44.]

The author gives an account of his experiences with oriental sore, some 200 cases of which he has encountered since 1938 at the hospital skin clinic at Ankara. Most of the cases of this disease in Turkey come from Central or Eastern Anatolia. The majority of the cases show characteristic sores, but a number develop atypical lesions as a result of secondary bacterial infections. Thus, cases resembling syphilis, tuberculosis, erysipelas and pyogenic skin infections are encountered. Where secondary bacterial invasion occurs local antibacterial treatment by antiseptics is indicated, while prontosil may be given internally. At the same time anti-leishmania remedies, such as neostibosan, fouadin or tartar emetic, are employed. In some cases to bring about healing X-ray treatment or electrocoagulation have been used.

C. M. W.

AKAN (Vefik Vassaf). Ueber Leishmaniose in der Türkei. [**Leishmaniasis in Turkey.**]—*Türkische Ztschr. f. Hyg. u. Experim. Biol.* Ankara. 1940. Vol. 2. No. 1. pp. 67–71. With 5 figs. [Turkish version pp. 58–66.]

A short account of leishmania infections and the life history of the causative organism. No new information is given except in the statement that certain observers have successfully treated oriental sore with atebrin.

C. M. W.

PESTANA (Bruno R.), PESSÔA (S. B.) & CORRÊA (Aniceto). Notas sôbre a leishmaniose no município de Marília, estado de São Paulo (Alta Paulista). [**Leishmaniasis at Marília, São Paulo.**]—*Arquivos de Hig. e Saúde Pública.* 1940. Jan. Vol. 5. No. 8. pp. 15–18. English summary (7 lines).

VILLELA (Francisco). Dados estatísticos sôbre a leishmaniose das mucosas em Araçatuba, estado de São Paulo. [**Statistics of Muco-Cutaneous Leishmaniasis in Araçatuba, São Paulo.**]—*Ibid.* pp. 21–24. English summary (6 lines).

PESTANA (Bruno Rangel) & PESSÔA (S. B.). Leishmaniose tegumentar autóctone no município de São Paulo. [**Endemic Cutaneous Leishmaniasis in the Town of São Paulo.**]—*Ibid.* pp. 27–33. With 3 figs. English summary (6 lines).

PESSÔA (S. B.) & PESTANA (B. Rangel). Sôbre a disseminação da leishmaniose tegumentar no estado de São Paulo. (Resultado de um inquérito realizado nos "Centros de Saúde" do Interior.) [**Dissemination of Cutaneous Leishmaniasis in the State of São Paulo.**]—*Ibid.* pp. 37–46. With 2 maps. English summary.

—— & ——. Leishmaniose tegumentar urbana. [**Urban Cutaneous Leishmaniasis.**]—*Ibid.* pp. 49–55. With 1 map. [11 refs.] English summary.

This series of papers is concerned with the epidemiology of mucocutaneous and cutaneous leishmaniasis in the State of São Paulo. The area covered can be divided into four sections according to the incidence of the disease. These are zones of high, moderate and low endemicity and a zone which is free from the disease. The distribution of the infection according to age, sex, nationality and residence has shown that intimate contact with wooded country is not always a necessary condition for acquiring it. A special study of rural and urban districts within the zone of high endemicity has shown that only in the one town, Araçatuba, were any considerable number of cases met with. It is admitted that infections occur occasionally in this town, owing to the density of the transmitting agents (species of *Phlebotomus*) in its periphery, but investigators have shown that the majority of the cases have come from the rural districts. On the whole, leishmaniasis in the State of São Paulo cannot be regarded as a problem of urban hygiene. *C. M. W.*

GEIMAN (Quentin M.). **A Study of Four Peruvian Strains of *Leishmania brasiliensis*.** [Paper read at 16th Ann. Meeting of American Society of Parasitologists. Abstract taken from *Supp. to Jl. Parasitology.* 1940. Dec. Vol. 26. No. 6. pp. 22–23.]

"Sixty-nine cases of cutaneous and nine cases of mucocutaneous leishmaniasis, commonly called *utá* and *espundia* respectively, were studied in Peru. Thirty-nine cases of *utá* were suitable for attempts to discover and isolate the causative organism. Stained films from 5 patients and cultures from 4 were positive for *Leishmania brasiliensis*. Scrapings of cutaneous lesions were inoculated directly into white mice and one dog on two occasions. No infections resulted. Swiss mice, dogs and monkeys (*Macaca mulatta*) were given subcutaneous or intraperitoneal inoculations from cultures. No gross lesion was produced or found at autopsy of the mice but positive cultures of *Leishmania* were recovered from the spleen of three mice one month after

intraperitoneal inoculation. One dog developed typical *utá* on the nose and ear from which organisms were recovered in stained films and cultures. A biopsy specimen from the infected dog's nose produced a lesion when implanted in the nose of a second dog. The relative infectivity of *L. tropica* (1 strain, isolated in Algiers in 1928) and *L. brasiliensis* (4 strains) for the chorio-allantoic fluid of the developing chick embryo was determined. The fluid of 5–9 day embryos was easily infected with *L. tropica* and it contained great numbers of actively motile organisms at the end of 3–5 days. No invasion of the membranes and the blood stream occurred. Twenty-six serial passages were made during a period of four months. Initial inoculation of *L. brasiliensis* under identical conditions produced no massive infection but only a morphological change, loss of motility, and a survival of the original organisms to the second passage. No tissue or blood stream invasion was detected."

AMOEBIASIS AND OTHER FORMS OF DYSENTERY.

Précis of Abstracts in this Section.

Howell and Knoll (p. 267) point out that amoebiasis in the young in the United States is by no means rare; they have found infection in over 3 per cent. of children and in 5·2 per cent. of adults examined. They describe the symptoms and treatment given. Tsuchiya and Jean (p. 267) found *E. histolytica* in 12 of 562 students at St. Louis, Missouri; none gave a history of symptoms attributable to the infection. Barcelos (p. 267) reports an outbreak of amoebic dysentery in the island of Carvalho.

By experiments with dogs, Tobie (p. 268) has shown that strains of *E. histolytica* from carriers are pathogenic, and argues that the so-called healthy human carriers should be regarded as clinically infected and should be treated. Borland (p. 268) holds the same opinion and does not agree with the view held by some workers that *E. histolytica* may live in man as a harmless commensal.

Bercovitz (p. 269) has shown that in autopsy material cells found in the bowel contents are the same as those found in scrapings of the mucosa from the same areas. In the bowel discharges of patients suffering from a variety of pathological conditions there may be large cells which may be confused with *E. histolytica*. Polymorphonuclear leucocytes and epithelial cells may also be found.

Mateer *et al.* (p. 270) give in detail their method of treating amoebiasis by oral administration of carbarsone, and by enemata of yatren. This gave 97 per cent. of cures in acute, chronic and latent cases.

Craig (p. 271) writes of the value of diodoquine (which is described) not only in treatment but also as a temporary prophylactic for those passing through areas where amoebiasis is endemic. It can be taken in large doses over a considerable period without ill effects.

HUMMEL (p. 272) reports a patient with an amoebic granuloma of the rectum and a balantidial infection of the sigmoid. Treatment, which included diodoquin, was successful against both conditions.

GHOSH (p. 272) states that a number of skin infections, intractable to usual treatment, cleared up when the finding of amoebae in the stools led to the administration of emetine or stovarsol.

In *Nature* (p. 272) is given a note on new official standard for the alkaloidal content of ipecacuanha.

NAIDU (p. 273) reports two cases of poisoning by Kurchi bark in children.

SILVERMAN and ST. MARTIN (p. 273) give clinical details of patients with liver abscess.

MCGRATH *et al.* (p. 274) discuss the mechanism of fat absorption in relation to a patient who had symptoms of steatorrhoea. The duodenal contents contained vast numbers of *Giardia intestinalis*, the normal mucous membrane pattern, seen at X-ray, was almost obliterated and at post mortem it was found that the valvulae conniventes were practically absent, the villi and crypts being almost denuded of surface epithelium. There was no evidence that Giardia had penetrated the villi and crypts, but the authors ascribe the symptoms of idiopathic steatorrhoea to injury of the epithelial lining of the small intestine.

VOTRINA (p. 275) writes of the efficiency of atebrin in the treatment of giardiasis, especially when the clinical manifestations are those of enterocolitis, in which case there is a general improvement in the condition of the patient. If the symptoms are those of cholecystitis there is no immediate improvement. LOVE and TAYLOE (p. 276) record success in the treatment of infections with *G. intestinalis* by means of atebrin.

NELSON (p. 276) has been able to cultivate *Balantidium coli* in a medium of one part of contents of the caecum of the pig, and nine parts of Ringer's solution.

Bacillary Dysentery.—OUYANG (p. 277) reports on bacillary dysentery in children in Peiping. The incidence was highest in summer and in the poor and ill-nourished. Clinical details are given; the commonest complication was bronchopneumonia, but thrombocytopenic purpura was seen in some. In treatment emphasis is laid on the administration of saline, subcutaneously or intraperitoneally, to combat dehydration, or of glucose intravenously, and on blood transfusion. Polyvalent antidysentery serum is of doubtful utility.

In reporting on bacillary dysentery in the German army during the campaign in Poland, OTTO (p. 278) points out that epidemics were noticeably associated with plagues of flies, and that the disease was spread in hospitals by direct contact. He describes abortive, mild, moderate and severe types in considerable detail and gives a long list of complications. Infection was principally due to Flexner bacilli. He gives details of treatment, which was largely concerned with fluid and salt replacement and with diet, but there is no mention of oral saline treatment, and the sulphonamides were not used. Serum was valuable if given early.

REITLER and MARBERG (p. 280) report remarkably good results in the treatment of bacillary dysentery with sulphapyridine alone. Details of the causative organisms and of the progress under treatment are given.

C. W.

HOWELL (Katharine M.) & KNOLL (Elta W.). **Amebiasis in Infants and in Children.**—*Amer. Jl. Dis. Children.* 1941. Jan. Vol. 61. No. 1. pp. 54–63. [16 refs.]

There is a widely-held idea that amoebiasis in the young is very rare, except in the tropics. This is erroneous, as OSLER and others in the United States have shown. H. F. HARRIS stated that one child is infected to every ten adults who acquire the disease. The authors have examined the stools of 408 children at their hospital, during the three years 1937–39, and found 13 infected. During the same period 55 were found among 1,044 adults examined (5·2 per cent.). Between 1929 and 1939 inclusive 18 children were found with amoebiasis, 12 were boys, 6 were girls; their ages ranged between 8 months and 13 years. Some had acute abdominal pain, nausea and fever, simulating acute appendicitis; others were subject to "colitis" or intestinal disturbance at intervals over a period of years, others again had no localizing symptoms and were discovered accidentally among those in hospital for other diseases such as pseudohypertrophic muscular dystrophy, inguinal hernia, enlarged tonsils and adenoids.

Under treatment the symptoms of amoebiasis rapidly cleared up, two were given emetine hydrochloride, the others carbarsone. The authors do not agree "that cysts of E. histolytica in stools indicate the carrier state, with the host-parasite equilibrium established, and that the presence of trophozoites indicates acute amebiasis," for in some cases cysts would be found one day, a few days later they might see precysts and trophozoites, while all forms might be seen on another occasion. Reference is made to the stools of 105 children examined at a Chicago orphanage, among whom there were five with *E. histolytica* (4·8 per cent. as compared with 3·18 at the Sarah Morris Hospital), thus bearing out the view that the incidence of amoebiasis is greater in institutions than among the general public. *H. H. S.*

TSUCHIYA (H.) & JEAN (J. Ted). **The Incidence of Intestinal Protozoa among Freshman Medical and Dental Students with Especial Reference to Amebiasis.**—*Amer. Jl. Trop. Med.* 1940. Nov. Vol. 20. No. 6. pp. 803–808.

An examination of 562 medical and dental students at the School of Medicine at Saint Louis, Missouri, has revealed an *Entamoeba histolytica* infection in 12. Of these, 6 were in students from Missouri, 2 from Illinois and one each from New York, New Jersey, Montana and Utah. The number of students from some of the States was, however, small, so that little significance can be attached to some of the negative results. Other intestinal protozoa were also found—with the exception of *Dientamoeba fragilis*. Not one of those found to harbour *E. histolytica* revealed any history of dysentery or symptoms attributable to the infection. The report once again produces evidence that amoebiasis is cosmopolitan in distribution. *C. M. Wenyon.*

BARCELOS (Vasco de Freitas). Um surto de disenteria amebiana na Ilha do Carvalho, em Neves. [**An Outbreak of Amoebic Dysentery in the Isle of Carvalho, Neves.**]—*Arquivos de Higiene.* Rio de Janeiro. 1940. June. Vol. 10. No. 1. pp. 109–126. With 5 figs. & 1 chart.

This outbreak involved 30 among 102 inhabitants [according to two tables 30 cases, in another 31, in the letterpress 34 are mentioned,

and the inhabitants, in one table, total 102, in another they are given as 115, by a wrong addition which really amounts to 125] and seems to have been due to a combination of causes. A carrier or cyst passer was found who came into fairly intimate contact with the others; the sanitation left much to be desired, the water was unprotected, effluent passed to that part of the shore whence people bathed, flies were abundant, and so forth. The first case was observed on December 27th, 1938, the only one that week, thereafter in successive weeks were 4, 11, and 15 notified respectively. Treatment of the patients and ordinary sanitary precautions soon put an end to the outbreak.

H. H. S.

TOBIE (John E.). **Pathogenicity of "Carrier" Strains of** *Endamoeba histolytica* **in the Experimental Dog.**—*Proc. Soc. Experim. Biol. & Med.* 1940. Nov. Vol. 45. No. 2. pp. 691–693.

This investigation had in view the experimental determination of the pathogenicity or non-pathogenicity of the "healthy carrier" strains of *E. histolytica, i.e.* strains from persons harbouring the amoeba but showing no clinical symptoms. The strains were obtained from a group of orphan children who had shown no symptoms of dysentery and not even diarrhoea. The cysts or trophozoites were obtained from the faeces and dogs were inoculated intragastrically with cysts or intracaecally with trophozoites, isolated in culture. Twenty-six dogs were inoculated with 16 different "carrier" strains and all became infected and showed clinical signs and symptoms or the intestinal lesions of dysentery, such as extensive denudation of the mucosa, ragged, round and slit-like ulcers, or typical pin-point lesions. In other words all the "carrier" strains were pathogenic to dogs, and if the conditions in the dog are comparable with those in man, all persons harbouring the amoeba have some lesions in the bowel and there is, *sensu stricto*, no such thing as a "healthy carrier condition in man"; "carrier" strains of the entamoeba are pathogenic and the so-called healthy human carriers should be regarded as clinically infected and be treated.

H. H. S.

BORLAND (James L.). **Factors in the Diagnosis of Intestinal Protozoa in Man and in the Interpretation of the Findings.**—*Amer. Jl. Digestive Diseases.* 1940. Oct. Vol. 7. No. 10. pp. 401–406. With 1 graph. [21 refs.]

Writing from Florida the author discusses the difficulties in diagnosis of intestinal protozoal infections and in arriving at decisions regarding the pathogenicity of those found to be present. As regards *Entamoeba histolytica* the opinion has been growing that this amoeba may at any time live as a harmless commensal in the intestine, but the author holds that it has not yet been demonstrated that any person infected has been free from intestinal lesions. The precautions which have to be taken to ensure accurate diagnosis, such as the supply to the laboratory of material suitable for examination, are emphasized. It is particularly noted that infected individuals do not of necessity pass protozoa in the stools every day, so that conclusions based on a single negative examination are apt to be misleading. When every precaution has been taken, it still has to be recognized that "reports

coming from a technician who lacks long and specific protozoological training, regardless of his competency in other microscopic fields, had best be discarded and conclusions drawn from clinical observations alone." *C. M. W.*

BERCOVITZ (Z.). **Studies in Cellular Exudates of Bowel Discharges. I. Control Observations in 1,123 Patients, 7 Autopsies, and 3 Dog Experiments.**—*Jl. Lab. & Clin. Med.* 1940. May. Vol. 25. No. 8. pp. 788–795. With 2 figs. [12 refs.]

——. **Studies in the Cellular Exudates of the Bowel Discharges. II. The Differential Diagnosis of Amebiasis. Types of Cells found in Bowel Discharges of Patients with Bowel Complaints.**—*Amer. Jl. Digestive Diseases.* 1940. Mar. Vol. 7. No. 3. pp. 93–101. With 17 figs.

In the first paper the author has made a thorough attempt to weigh up the significance from a diagnostic viewpoint of cellular exudates in bowel discharges. After reviewing the earlier work, mainly performed during the last war, on this subject, he concludes that the suggestion of WENYON & O'CONNOR on the relationship of cellular exudates to ulcerative colitis and other types of bowel complaints has received ample confirmation.

These special studies which have been carried out during the past four years have established the fact that, whenever pathogenic changes take place in the bowel mucosa, various types of cell will be found in the discharge, and conversely, when no cells are found in the bowel discharge no pathological condition is present. As a preliminary a series of observations was undertaken to determine whether a cellular exudate could be found in the discharge of a patient whose bowel functions were reported as normal, and, in order to establish a reliable check on these observations, examinations were made in a series of autopsies, and also upon a group of 1,123 patients selected at random, under conditions where no complaints were made on the functions of the gastro-intestinal tract.

The specimens examined consisted firstly of normally passed stool and secondly of the diarrhoeal discharge following dosage with Epsom salts. So that freshly passed warm specimens could be studied patients were asked to come to the laboratory to evacuate their bowels after administration of the salts. The human autopsy material, including bowel contents and scrapings from several locations along the gastro-intestinal tract, was examined and in each case scrapings from the bowel wall were taken from the same place as the bowel contents and were fixed in 10 per cent. formalin. The investigations were directed to ascertain whether or not the cells found in the contents corresponded exactly with those found in the scrapings from the same area.

In order to deal satisfactorily with the problems raised by possible post-mortem degeneration, three dogs were killed by intravenous and lethal doses of amytal. The abdomens were opened immediately and their bowels were studied before any post-mortem changes could possibly take place.

Out of an examination of 2,158 specimens of normal and diarrhoeic (Epsom salts) stools only 11 were positive for cells; no further investigation of their implication was carried out. From a study of the autopsy material it was discovered that cells found in the bowel

contents were the same as those found in scrapings from the same areas. It could therefore be affirmed that these cells were the result of post-mortem degeneration, and these findings were in complete agreement with those of SCHMIDT & STRASSBURGER in their monograph in 1910 (*Die Fäzes des Menschen*).

The second paper elaborates this study in relation to pathological discharges from the bowel. Bercovitz has applied the method of colonic irrigation—a tepid colonic irrigation with normal saline is continued until the return flow is entirely clear of faecal matter. The terminal mucus is obtained for examination. The patient should be given a series of three such irrigations ; the first two being discarded. He prepared 179 patients in this manner and altogether 248 specimens were studied. *Entamoeba histolytica* was found in 14, which constituted 7·7 per cent. of the total number.

The advantage of studying this type of specimen lies in the fact that, even though a cellular exudate may be present, the amoebae can be readily visualized and identified. These amoebae when freshly passed exhibit all their characteristics and further details can be brought out by staining with Lugol's solution.

Bowel discharges were examined from a series of 200 patients suffering from a variety of pathological bowel conditions and the types of cells observed were particularized. Large cells with prominent nuclei, 20–30μ and even in some cases 150μ, are apt to be confused with *E. histolytica*; when stained with Delafield's haematoxylin and eosin the nuclei appear more solid and do not exhibit the same characteristics as in fresh wet-fixed specimens. [These are evidently the cells described by the reviewer and others. See this *Bulletin*, 1918, Vol. 12, p. 427.] Polymorphonuclear leucocytes are readily seen, and in fresh unstained preparations the nuclei appear as open rings with usually two or three in a single cell which may be confused with the cysts of *E. histolytica*. Epithelial cells with oval or rounded nuclei, solid or ringed, are frequently found and can be well demonstrated with methylene blue. [These papers are illustrated by a series of excellent photomicrographs which, unfortunately, do not bring out the minor details exemplified in drawings. These include a series from chronic ulcerative colitis, in which the cell picture is similar to that of acute bacillary dysentery, but no explanations are forthcoming as to any means of differentiating these two dissimilar conditions.]

P. Manson-Bahr.

MATEER (John G.), BALTZ (James I.), MARION (Donald F.) & HOLLANDS (Robert A.). **The Treatment of Amebiasis by a Combined Method —Statistical End Results. (Oral Administration of Carbarsone and Retention of Enemata of Chiniofon.)**—*Amer. Jl. Digestive Diseases.* 1940. Apr. Vol. 7. No. 4. pp. 154–159.

The authors have observed 104 patients with uncomplicated amoebiasis treated by a combination of carbarsone and yatren. The former was given orally in doses of 0·25 gm. twice daily for ten days, and the latter as a retention enema on alternate mornings for the same period, the yatren being preceded by a cleansing saline enema of 750 cc. They give in detail the ritual of the enema. On enema days no breakfast is allowed, but at 8 a.m. the patient has the wash-out. At 9 a.m. 250 cc. of a 2·5 per cent. aqueous solution of yatren are run in with the patient in the genu-pectoral position. The patient remains

in this position for five minutes so that some at least of the yatren reaches the ascending colon. He then drops on the right side and stays thus for half an hour (to retain the fluid in the caecum and ascending colon), then on to the back for half an hour, next on to the left side for the same time, then from 10·35 a.m. to 1 p.m. on the back again. Patients were kept under observation for three years or more. Stools were obtained by warm saline enema or by a saline cathartic weekly for four weeks after completion of the course of treatment, then monthly for five months and thereafter every six months.

The 104 cases are divided into five groups: (1) Those with acute amoebic dysentery, 20 in number. (2) Chronic relapsing dysentery (19) with history of previous acute or subacute attacks. These two groups were, therefore, suffering from acute amoebiasis. (3) Carrier or latent cases (25) without any colon symptoms. (4) Latent cases with "chronic irritable colons." (5) Another type of latent amoebiasis, with small pin-point ulcers in the colon. [The reviewer cannot follow the authors in their statement: "The 65 cases in the last three subgroups were cases of clinically 'latent' amoebiasis"; so far good, but "In this latent group of 65 cases, the 40 cases in the last two clinical subgroups had colonic symptoms not of amoebic etiology." If they were cases of latent amoebiasis with irritable or ulcerated colon, by what criteria is the decision reached that the symptoms were not of amoebic aetiology?] Three of the 104 showed a recurrence but this was cured by giving vioform. No patient showed any unfavourable reaction. The drugs hitherto used alone have not been credited with more than a 90 per cent. success; of the 104 dealt with, all cleared at once and were free of amoebae, except the three already mentioned which relapsed, in other words the combined drugs gave 101 cures out of 104, or 97 per cent. *H. H. S.*

CRAIG (Charles F.). **The Medicinal Prophylaxis of Amebiasis.**—*Amer. Jl. Trop. Med.* 1940. Nov. Vol. 20. No. 6. pp. 799–801.

It is too much to expect that drugs found useful in the treatment of amoebiasis could be taken constantly to protect those living in an endemic district, but their temporary use to safeguard those passing through such a district or making a short stay is a different matter. Prophylaxis by avoidance of all uncooked food and unboiled water, however desirable theoretically, is not always feasible. Three drugs are worth considering: carbarsone, chiniofon and diodoquin. The first, though an efficient amoebicide, is an arsenical preparation and too toxic to be taken except under medical supervision. The second, though less toxic, in some persons causes a diarrhoea; the third can be taken in large doses over a considerable period without ill effects.

"Diodoquin (5,7-diiodo-8-hydroxyquinoline) is a compound in which the sodium sulfonate radical of chiniofon has been replaced with a second iodine atom, forming a double iodine compound." Chiniofon is a mixture of 7-iodo-8-hydroxyquinoline-5-sulphonic acid, 4 parts by weight, and sodium bicarbonate 1 part. It contains 28·2 to 29·6 per cent. of iodine, whereas diodoquin contains 63·9 per cent. of iodine and it is on this that its amoebicidal properties depend. It is put up in tablets of 0·21 gm. (3·2 grains) and for treatment of infection 7–10 tablets are taken daily, the smaller dose for latent (cyst-passers) and mild cases. For prophylaxis this is the dosage recommended, two tablets after breakfast and lunch, three after dinner daily (for adults)

for 20 days. If the stay in the endemic region is less than 20 days, it is nevertheless advisable, says Professor Craig, to complete the course. If the person has to stay longer the course may be repeated after a week's interval. *H. H. S.*

HUMMEL (H. G.). **Amebic Granuloma of the Rectum and Balantidiasis in the Same Patient.**—*Amer. Jl. Digestive Diseases.* 1940. Apr. Vol. 7. No. 4. pp. 178–179. [17 refs.]

Amoebic granuloma of the large intestine, though not common, has been reported sufficiently often for the tropical practitioner to be on his guard and not to jump to the conclusion that the owner is suffering from a malignant growth. The patient, whose case is here recorded, was a man of 49 years who had suffered from chronic diarrhoea (10–20 stools in 24 hours) and had lost 40 lb. in weight in the twenty years of his complaint. He had tenderness over the descending colon; blood examination gave r.b.cs. 3,408,000, white cells 9,400 per cmm., haemoglobin 77 per cent., colour index 1·1. Sigmoidoscopy revealed, 7 inches from the anus, a greyish-pink granulomatous growth the size of a large walnut, edges nodular and with necrotic areas on the surface; there were discrete punched out ulcers in the sigmoid. Scrapings from the former showed many *E. histolytica* and from the latter *Balantidium coli*. Treatment consisted of a high caloric, low residue diet and 500 units of vitamin B and diodoquin (a di-iodohydroxyquinoline compound containing 64 per cent. iodine) 0·21 gm. (ten tablets) daily for ten days. When seen again after this interval the patient had gained 10 lb. in weight, stools were reduced to two daily, abdominal pain had disappeared, sigmoidoscopy revealed a normal bowel, no ulcers or granuloma, but an irregular scar, 4 cm. in diameter, at the site of the former tumour. The author states that he has used diodoquin in forty-one consecutive cases of amoebiasis with excellent results and it seems to have equally gratifying results on amoebic granuloma and balantidiasis. *H. H. S.*

GHOSH (H.). **Inhibitory Influence of Chronic Amoebiasis on Immunity against Bacterial Infection.**—*Jl. Indian Med. Assoc.* 1940. Aug. Vol. 9. No. 11. p. 541.

The author states he has met with several cases of local skin affections such as scabies, staphylococcal eczema, streptococcal pustules, all of which have resisted the usual methods of treatment and the latter two the use of vaccines, but which cleared up when the finding of amoebae, in vegetative or cystic form, in the stools led to the administration of emetine and stovarsol.

On these grounds it is held that "amoebiasis plays a great rôle in the chronicity of bacterial skin infection by exerting an inhibitory influence on the natural formation of antibodies." *H. H. S.*

NATURE. 1940. July 27. Vol. 146. No. 3691. p. 125.—**The B.P. Standard for Ipecacuanha.** [News and Views.]

In this note attention is drawn to a notice in the *Gazette* of July 5th, 1940, in which is announced an alteration in the standard for the alkaloidal content of ipecacuanha. The B.P. 1932 requires the root to contain not less than 2 per cent. of the total alkaloids calculated as

emetine, of which not less than two-thirds consists of non-phenolic alkaloids calculated as emetine. The change now made is the substitution of "three-fifths" for "two-thirds." This slight change will have a marked effect on the availability of the drug since the 1932 test excluded large importations from Bahia and Minas Geraes which will now to a great extent conform to the new B.P. standard. A reduction in cost is to be expected and the new regulation will probably be of importance in regard to supplies of emetine. *C. W.*

NAIDU (S. Rajagopal). *Holarrhena antidysenterica* **Wall.**—*Madras Ann. Rep. Chemical Examiners Department for Year 1939.* pp. 3–4.

The author reports poisoning by kurchi (or conessi) bark given as a purgative to two children. Death was apparently due to heart failure, and extracts of alkaloids were obtained from the viscera and from specimens of the plant used, *Holarrhena antidysenterica.* These alkaloids gave the same results with various chemical tests.

Recent clinical experiences have led to the adoption of this plant as a remedy in dysentery, but its alkaloids are known to be poisonous. Indiscriminate use, therefore, is highly dangerous. *C. W.*

SILVERMAN (Daniel N.) & ST. MARTIN (Roy J.). **Early Diagnosis and Treatment of Amebic Abscess of the Liver.**—*New Orleans Med. & Surg. Jl.* 1940. Aug. Vol. 93. No. 2. pp. 90–92.

For treatment of amoebic hepatitis and hepatic abscess to be effective without operation, early diagnosis is all-important. Often, and particularly among those physicians who have not had tropical experience, the diagnosis is excluded on the grounds that the patient does not give a history of previous dysentery. [We must remember also that amoebiasis of the intestine may be associated with symptoms varied and vague, see MAYER, this *Bulletin*, 1940, Vol. 37, p. 734].

The authors give details of four patients with liver abscess, three of them being treated medically, the fourth [a doubtful case in the reviewer's opinion] died after operation. The first was a man of 51 years who developed an enlargement of the liver with leucocytosis of 32,000 per cmm. *during* an attack of dysentery. Improvement followed the use of emetine. [Presumably, a history of a previous attack of dysentery was enquired into, but no statement to that effect is made. Incidentally, the stool examination was negative. The diagnosis in this case seems to have been made on the effects of emetine.] The second was a man of 42 years who received treatment for amoebic dysentery (with stovarsol). A fortnight after the stools were found free from *E. histolytica*, he developed signs of liver abscess, which improved with emetine injections. The third was a woman with signs of hepatitis which cleared up on treatment with emetine. No entamoeba were seen in the stools, but the patient gave a history of previous treatment for "mucous colitis." The fourth is designated "amebic abscess of liver without history of dysentery and with negative stool evidence" [but in the notes given in the text, no evidence of the abscess having an amoebic origin is adduced]. The patient

had undergone a cholecystectomy [cause not stated] and 19 days later began to develop an abscess of the liver. Operation was performed but death occurred with general peritonitis. *H. H. S.*

McGrath (John), O'Farrell (P. T.) & Boland (S. J.). **Giardial Steatorrhoea. A Fatal Case with Organic Lesions.**—*Irish Jl. Med. Sci.* 1940. Dec. pp. 802–816. With 8 figs. on 4 plates. [27 refs.]

The case recorded is remarkable in so far as it closely resembled a typical case of idiopathic steatorrhoea. The essential facts are preceded by a physiological exposition on the chemistry of lipoids and the process of their absorption. There is evidence that fatty acids are assisted through the mucosa by the aid of phosphatides and that the presence of unsaturated fatty acids is necessary for the absorption of other fatty acids and for excretion of waste products.

Phosphorylation, a process which enables fat to be ingested, takes place on the surface of the epithelial cells covering the villi. The absorption of fats will therefore be lessened, or prevented, if the surface epithelial cells are damaged or destroyed. The failure to absorb fats will be in direct proportion to the extent of this destruction. Therefore increased faecal fat content may arise in three different ways :—(*a*) the digestion of fats may be deficient owing to obstruction, failure of bile and lipase, or because of intestinal hurry, or (*b*) the ultimate absorption of fats may fail owing to destruction of the lacteals and mesenteric lymphatics, or (*c*) there may be interference with absorption of fats in the mucosa of the intestine. In the first type the stools will contain a large proportion of neutral unsplit fat, whilst in the other two the faecal fat is mostly split.

In the present instance there was interference with fat absorption (as in true idiopathic steatorrhoea) and also similar interference with carbohydrate metabolism. The patient was a man of 40, of good physique and weighing 14 stone. At first there was loss of weight accompanied by signs of subacute cholecystitis. Cholecystectomy was performed (unfortunately the gall bladder was not pathologically examined). Subsequently, symptoms of steatorrhoea became acute, with anaemia, clubbing of fingers and increasing dehydration. Death occurred within five months. On two separate occasions duodenal contents, obtained by intubation, were found to contain vast numbers of active *Giardia intestinalis*, and it is noteworthy that, in spite of intensive search, none of these flagellates or their cysts was discovered in the faeces.

The radiological appearances of the intestinal tract resembled those described by Camp (1934) and Kantor (1939). The normal mucous membrane pattern in the jejunum is to a great extent obliterated, the upper loops being most frequently involved and the destruction of the *valvulae conniventes* so complete as to cause the "*moulage sign*," resembling a tube into which wax had been poured. [This section is illustrated by excellent radiographs.] In short the findings were very suggestive of idiopathic steatorrhoea. At this stage the general features of the case seemed to point to a diagnosis of Gee-Thaysen disease (idiopathic steatorrhoea) on the general grounds of emaciation, dehydration, clubbing of fingers, irregular diarrhoea, oedema of the legs, hyperchromic anaemia, hypochlorhydria, low fasting blood-sugar, flat blood-sugar tolerance curve, diminution of serum, calcium, normal

serum phosphorus and phosphatase, marked excess of faecal fat with normal splitting, haemic heart murmur and X-ray findings.

The possible relationship of Giardia to intestinal disease is next considered in a review of the literature with special reference to its occurrence in the biliary tract and duodenum, especially the findings of ROMANO *et al.* (1938) [this *Bulletin*, 1939, Vol. 36, p. 605], EUSTERMAN (1939) and BONANNO (1940), upon which it is inferred that heavy infestation with this parasite may cause severe or possibly fatal illness. Moreover, MILLER has described a syndrome of giardiasis in children in England which closely resembles coeliac disease. WESTPHAL & GEORGI operated upon a case of cholecystitis due to *Giardia intestinalis* and found the walls of the gall bladder thickened and hyperaemic.

At autopsy the main pathological changes were in the small intestine. The walls of the duodenum and upper part of the jejunum for about twelve inches were very thin. The *valvulae conniventes* were practically absent. In sections the villi and crypts appeared to be denuded of surface epithelium. In general, the villi reminded one of a gaunt dead tree with rotting branches from which the bark had peeled. Further along the jejunum the villi tended to disappear altogether in places, giving rise to the appearance of bald patches. The ileum in many areas was thickened with stenosed lumen and for a considerable extent the mucous membrane was entirely absent, in fact the condition closely resembled regional ileitis (Crohn's disease). The pathological changes did not extend beyond the caecum.

In scrapings made from the surface of the mucosa of the duodenum and jejunum and from ulcerated areas of the ileum multitudes of Giardia were found. The enlarged mesenteric glands were due to hyperplasia ; no evidence was obtained in sections that Giardia had penetrated the villi and crypts of the intestinal mucosa. It is significant that lesions similar to those of regional ileitis have been previously ascribed to giardiasis by SHAPIRO (1939) and BARBOUR & STOKES (1936).

The clinical findings, which so closely resembled idiopathic steatorrhoea, were caused by injury to or destruction of the epithelial lining of the small intestine, giving rise to the syndrome of " chronic jejuno-ileal insufficiency " [BENNETT & HARDWICK, this *Bulletin*, 1941, Vol. 38, p. 7]. It is claimed that this is the first case of giardiasis recorded in Ireland.

[No further comment is possible, at this stage, but the detailed presentation of this thoroughly worked out case will undoubtedly stimulate further investigation into the pathogenicity of Giardia. In this connection it may be noted that the reviewer has already described a sprue-like syndrome in association with massive infection with Giardia. (*Dysenteric Disorders*, 1939, p. 267). References to the other workers quoted are given in the original paper.]

P. Manson Bahr.

VOTRINA (E. N.). Sur la question du traitement de la lambliose par l'acrichine. [**Treatment of Giardiasis with Acrichine.**]—*Sovietskoe Zdravookhranenie Turkmenii* [*"Soviet Health Protection of Turkmenia"*]. Ashkhabad. 1940. No. 1. [In Russian pp. 22–24. French summary (5 lines) p. 24.]

The author reports the results of treatment of 25 cases of Giardia infection with acriquine [atebrin]. In eleven of these the symptoms

are attributed to the presence of the flagellates alone, while in the remaining cases they may have been due to concomitant diseases (pellagra, sprue, ankylostomiasis). The clinical manifestations of giardiasis were of two types: (1) enterocolitis, and (2) cholecystitis. Though the author does not commit herself to any definite opinion as to the pathogenicity of the flagellate, she advocates treatment in all cases of infection, in view of the successful results obtained with acriquine. This drug was administered either intraduodenally or *per os*. In the first method 10 cc. of 2·5 per cent. solution of acriquine is introduced through a duodenal tube, followed 10 minutes later by 40 cc. of 33 per cent. solution of magnesium sulphate and afterwards by lavage with saline. The treatment is carried out 3-5 times with intervals of 2–3 days between each administration. When given by mouth the doses are 0·3 gm. *per diem*, the course being divided into two 5-day cycles and one 3-day cycle, the interval between the first and second cycle being 5 days, and between the second and third 10 days. The results of the treatment by both methods were similar. The flagellates disappeared from the stools and could not be recovered from the duodenal contents; but while in the cases with giardial enter-colitis there was a general improvement in the condition of the patients, in the cases with cholecystitis no immediate improvement could be observed. In those cases in which giardiasis was associated with other diseases the treatment likewise resulted in the elimination of the flagellates. In view of its simplicity, the author gives preference to the peroral method of administration of the drug. *C. A. Hoare.*

LOVE (Julian) & TAYLOE (Gordon B.). **Atebrine in the Eradication of** *Giardia lamblia*.—*U. S. Nav. Med. Bull.* 1940. Apr. Vol. 38. No. 2. pp. 239–242.

Three patients with *Giardia intestinalis* infection, two of whom suffered from diarrhoea and vague abdominal discomfort and one who had no symptoms, were treated with atebrin 0·1 gm. three times a day for five days. A single course eradicated the infection in two cases but in the other this result was not obtained till the course was repeated after a five days' interval. In a footnote to the paper two further successful cases are mentioned. It is concluded that atebrin is an effective agent for the treatment of *G. intestinalis* infections, which may cause clinical symptoms in some cases. *C. M. W.*

NELSON (E. Clifford). **An Intestinal Content Cultivation Medium. I. Methods of Preparation and Use and Data obtained in the Cultivation of** *Balantidium coli* **from the Pig.**—*Amer. Jl. Trop. Med.* 1940. Sept. Vol. 20. No. 5. pp. 731–745. [10 refs.]

A simple medium for the cultivation of *Balantidium coli* has been devised. It consists of a mixture of one part of caecal contents of the pig and nine parts of Ringer's solution. The mixture is first strained through a sieve and then through a funnel lined with absorbent cotton. The *p*H of the resulting liquid varies according to the *p*H of the caecal

contents from which it was prepared. The higher the *p*H the longer will the culture of the ciliate survive, for it dies when the *p*H falls to 5, as it does after varying intervals. The greatest length of life of a culture was 34 days. For some reason not yet understood the bacterial growth in the medium is self limited, so that bacterial overgrowth does not occur as in some other liquid media. It is thus possible to use the medium in large quantities. Flasks containing 200 cc. have maintained cultures for 34 days, yielding as many as 8,260 balantidia.

C. M. W.

OUYANG (George). **Acute Bacillary Dysentery in Infants and Children. An Analysis of 315 Cases.**—*Chinese Med. Jl.* 1940. Oct. Vol. 58. No. 4. pp. 456–472.

This interesting study is based on the records of patients admitted to the children's ward of the Peiping Union Medical College in eight consecutive years 1930–38. Sixty-six (20·9 per cent.) were under 12 months old, 124 (39·3 per cent.) between one and two years, and 54 (17·1) between two and three years; that is, 60·3 per cent. of the total 315 were under two years and more than three-fourths (77·4 per cent.) were under three years. The fatality rate was highest in the very young; half those attacked under one year died; 45 (36·2 per cent.) of those between one and two years. The incidence was noticed to increase in May, reach a peak in July and then decline during the next three months. The two chief strains of organism concerned were *Bact. dysenteriae* Shiga in 61, of whom 21 died; one of the mannite fermenting group in 127 of whom 34 died; these two were found associated in 8, one of whom died.

The incidence was higher among the poor and ill-nourished. The symptomatology was noteworthy. Usually the temperature rose suddenly at the onset, in some falling by crisis the next day although the toxic symptoms appeared to be severe; in others the fever rose and death occurred in 24–48 hours with hyperpyrexia. In others, again, irregular and remittent high fever was observed, lasting for 3–4 weeks, but in most the early rise soon subsided and a low grade fever around 38°C. would persist for a week or two. In all cases, blood could still be found in the stools a week or more after the temperature became normal. The number of stools might reach 30 and even 45 a day, often accompanied with pain and tenesmus. Blood was seen by microscope in 207 of 256 stools taken on admission; gross blood was not often seen. Nearly half the children (136, or 43·2 per cent.) vomited at the onset (no more in Shiga than in Flexner infections) and in some this was the main complaint for which the child was brought. Convulsions were present in 90, or 28·6 per cent., usually at the onset. In seventeen this was the chief complaint at the onset. Forty-one of the 90 were infected with one of the Flexner group, 13 with the Shiga organisms. The commonest and worst complication was broncho-pneumonia, which was seen in 58 of the cases and ended fatally in fifty-four. Another worth special mention was thrombocytopenic purpura, which was seen in four, all of whom died. The author explains the development of this complication by assuming it to be the result of the action of the bacterial toxin on the bone-marrow or the platelets and related to deficiency of vitamin C. Death,

however, was not averted in any of those attacked in spite of administration of ascorbic acid parenterally in large doses.

Treatment: No food, water only, was given for the first 24–48 hours; then in small amounts and gradually increased to a maintenance level. The body dehydration occurring in acute bacillary dysentery is of the nature of a medical emergency and may be combated by subcutaneous or intraperitoneal saline; the former was given in quantities of 100–200 cc. in each thigh by the gravity method, the latter in quantities of 200–350 cc. at a time. Glucose intravenously, 5 per cent. in normal saline in doses of 25 cc. per kilogram body weight gave good results. In very severe infections glucose was administered by continuous intravenous drip to 18 patients. Blood transfusions were performed in 114 patients, 15 cc. per kilo. body weight. During the first fortnight they are given with a view to combating toxicosis, after that for increasing general resistance and controlling secondary infections. Polyvalent antidysentery serum was given and the author states: "The effectiveness of . . . serum in controlling the infection is doubtful," but it was tried in nine patients only who were very ill with convulsions and temperatures of 40°–41°C. and five died within the first two days of the illness. The course of the disease in the other four differed little from that in others who recovered without serum treatment.

H. H. S.

OTTO (H.). Die Ruhr bei der Feldtruppe in Polen. [**Dysentery among the Troops in Poland.**]—*Klin. Woch.* 1940. Mar. 16 & 23. Vol. 19. Nos. 11 & 12, pp. 241–245; 272–276.

An investigation of 300 cases of dysentery at Radom [*i.e.* nearer the field than GANTENBERG's investigation in Berlin; see *Bulletin of War Medicine*, 1940, Sept., No. 1, p. 34]. The cases were diagnosed as Shiga or Flexner infections by agglutination; bacteriological diagnosis was often negative. Epidemics were noticeably associated with plagues of flies. Ants were not responsible. Excessive eating of raw fruit coincided in the same period (September 1939) with the prevalence of flies, and probably contributed to the aetiology, both by direct contamination and by setting up a mild intestinal catarrh. Direct contact also probably spread the disease among troops in the field, as it did to nurses in hospital. Exact bacteriological classification was not practicable.

It is stressed that any enteritic outbreak among troops should be very seriously viewed, as neglect is apt to be followed by a major disaster. The cases in this outbreak fell into four groups:—

Abortive cases.—One or two days of diarrhoea, no mucus or blood in the stools, or definite pain. Some cases were febrile. Remained in their units, able to work, and recovered in a day or two. Some severe cases started this way, and as the abortive type may be infectious, it is better to treat it as serious.

Mild cases.—With mucus and blood in the stools, moderate diarrhoea, a little pain, weakness, headache and anorexia. Very little pyrexia (only in one or two paradoxically constipated cases). A little tenderness in the sigmoid and at the flexures, no vomiting, pulse strong and regular, no dehydration nor complications, complete recovery after short convalescence.

Moderate cases.—Features arise from (1) toxaemia ; (2) local lesions in colon and small intestine ; and (3) defective intestinal function.

Severe prodromal symptoms ; paroxysmal attacks of vascular collapse, with lividity and small rapid pulse ; cerebral toxic collapse from oedema of the brain ; dehydration and toxic wasting ; severe haemorrhagic colitis, up to 20 stools a day, with blood, pus and mucus ; intestinal colic and abdominal tenderness ; high pyrexia ; defective absorption, leading to chloride deficiency and tetany. Duration about 3 weeks. Some cases of severe cerebral symptoms such as insomnia and psychoses, suicidal or catatonic, were seen in this Polish epidemic, although this is not usually described and patients with severe infection as a rule die without any mental deterioration. Many of these moderately severe cases had a past history of appendicitis or other gastro-intestinal illness. Some of the moderate cases relapsed and persisted in sub-chronic form with pyrexia and tachycardia. Convalescence of moderate cases took weeks or months. The patients became weak and thin and took a long time to gain weight.

Severe cases.—Severe headache and anorexia at the onset, but the disease may come on gradually and become grave only after it is established. High fever, falling before death ; severe diarrhoea and tenesmus, or constipation, followed by porridge-like diarrhoea. Stools were passed every ten or fifteen minutes ; bellies were sunken and tender ; liver and spleen not enlarged ; bladder often distended through spasm of sphincter. The appearance was that of severe illness, with sunken eyes, profound dehydration, *facies hippocratica* and emaciation to a skeleton. The picture is so like Simmonds' disease as to suggest that there is an endocrine disorder as well as dehydration. There may be cramps, as in cholera. Death may result from cardiac weakness with pulmonary congestion, or from sudden heart failure. A sudden change from muco-purulent stools to thin brown offensive fluid is a grave sign. Some of the rapidly fatal cases were stuporose or sleepy, though rational when roused ; this was probably due to the severe toxaemia. Another group of fatal cases appeared superficially to do well for three weeks, although a good clinician could see that the unsteady rapid pulse, occasional pyrexia, and continued slime and pus in the stools boded ill. They went suddenly downhill and died in twelve hours in spite of all known circulatory restoratives.

Complications.—Two cases of arthritis, relieved by salicylates. Three cases of suppurative parotitis, drained ; two died. (Parotitis appearing early is not serious, but later in a case it is a fatal sign.) Four cases of conjunctivitis of short duration were seen. Membranous pharyngitis, which responded to gargling with red wine, occurred in severe cases. Two cases of renal colic, apparently due to spasm of an empty ureter were met with. Gastritis and inflammation of the small intestine, with green stools, were features of some of the severe cases. In two patients jaundice occurred, with enlarged liver but without splenomegaly. Neither nephritis nor general peritonitis were seen, but in one patient there was fatal localized peritonitis. Development of paralytic ileus with constipation and distension was observed in one, and profuse intestinal haemorrhage in six. A few cases of bronchopneumonia and one of bronchitis with asthma were seen. Peripheral neuritis and trophic oedema were noted, and toxic hiccup was an ominous sign. Two patients developed furunculosis of the buttocks, and two prolapsus ani. Two cases of tetany, cured by intravenous calcium, were seen. Wounds in dysenteric patients healed badly.

The post-mortem appearances described suggest that the infection was mainly with Flexner bacilli.

Treatment.—Strict rest in bed is essential, leaving the bed-pan with the patient if necessary. If the patient were seen in the first six days a dose of castor-oil was given, but not calomel. Animal charcoal in multiple divided doses was useful. Tannalbin was not effective, and bismuth subgallate, like calomel, was liable to be absorbed and cause poisoning. Opium seemed to do more harm than good. Atropine and hot fomentations were effective for colic and tenesmus. Diet consisted of biscuits for not more than three days, followed by a progressively increasing soft, bland diet of cereals, eggs and milk. Cocoa, chocolate and red wine were given. Apple-pulp was used largely, up to 2 lb. a day. Lemons were also given freely, to provide vitamin C. Fluid was given in large quantities, mainly as tea or coffee; cold drinks were found to increase colic. Salt was added to all drinks. Soft cheese, liver sausage and honey were found useful additions to the diet. Full diet was started when the stools became semi-solid and free from pus, blood and mucus. Salines were given subcutaneously in doses of 250 cc. twice a day for dehydration, and for chloride loss 20–30 cc. of 20 per cent. sodium chloride intravenously. Circulatory failure was treated not only by stimulant drugs, but also by doses of 60 cc. of 25–50 per cent. glucose intravenously. Adrenalin was found useful for collapse. Bromides were better than morphine to make the patients comfortable, and barbiturates were found to be the best remedies for insomnia. Hiccup responded only to large doses of amidopyrine or to cocaine. Blood transfusion was used in only two cases, but it seemed to do good. Very little anti-dysentery serum was available, but it seemed very valuable if given within the first week.

Charles Newman.

REITLER (Rudolph) & MARBERG (Kurt). **Note on the Treatment of Acute Bacillary Dysentery with Sulphapyridine.** [Memoranda.]—*Brit. Med. Jl.* 1941. Feb. 22. pp. 277–278.

The results obtained by the authors were so astoundingly good that it is hoped that others will make trial of the method with a view to confirming their findings. So far only 20 patients are reported upon, but their infections were varied and all were clinically severe cases. They included 13 infections by Flexner-Y, 4 by Shiga, and one each by Strong, Sonne-E and Schmitz, all confirmed bacteriologically.

On the day of admission the patients were under observation, but not treated, in order that the conditions before and after treatment might be compared. On the second day sulphapyridine, two tablets (= 1·0 gm.) were given by mouth, with $NaHCO_3$ to counteract nausea, three to four times daily for 2 to 4 days, according to the effect produced; it was usually administered for 24 hours after the motions became formed. No other treatment was given.

Usually in 24 hours the temperature fell, the diarrhoea was reduced, and in most cases the stools were normal in 48 hours. (Three patients took 3 days and one 4 days.) Toxic symptoms were seen in two Shiga infections and one Flexner; these also rapidly improved. Stools were bacteriologically negative when they became formed and in no case so far has a relapse occurred [but the interval since "cure" is not stated].

The following table gives the results detailed for each patient :—

Table showing Results of Sulphapyridine Treatment of Bacillary Dysentery.

Case No.	Type of Dysentery	Day of Disease when Admitted	Motions per Day						Duration of Sulphapyridine Administration (Days)
			Observation Day	Day of Treatment					
				1st	2nd	3rd	4th	5th	
1	Flexner-Y	3	26	8	2	1	1	1	2
2	Flexner-Y	3	23	8	1	1	1	1	2
3	Shiga	6	29	13	8	3	2	1	4
4	Flexner-Y	2	46	52	10	3	3	1	4
5	Flexner-Y	2	34	38	19	0	1	1	3
6	Flexner-Y	2	19	30	4	2	1	1	3
7	Shiga	6	56	13	0	0	1	1	2
8	Flexner-Y	4	8	10	0	1	1	1	2
9	Sonne-E	6	15	11	4	1	1	1	2
10	Flexner-Y	9	14	4	3	2	1	1	3
11	Flexner-Y	3	18	16	0	1	1	1	2
12	Strong	1	9	12	2	1	1	1	3
13	Flexner-Y	4	14	16	5	1	1	1	3
14	Flexner-Y	1	8	15	6	1	1	1	3
15	Shiga	4	30	26	35	19	6	2	4
16	Flexner-Y	1	30	12	4	0	1	1	3
17	Schmitz	2	8	14	4	2	1	1	4
18	Flexner-Y	2	8	9	6	2	3	1	4
19	Shiga	5	30	19	8	1	2	1	3
20	Flexner-Y	2	18	20	2	0	1	1	3

[See also this *Bulletin*, 1940, Vol. 37, p. 868.] *H. H. S.*

BERIBERI AND OTHER VITAMIN DEFICIENCIES.

Précis of Abstracts in this Section.

Fehily (p. 282) quotes Japanese work to show that the milk of women suffering from beriberi is toxic to their infants and produces infantile beriberi when the reserves of vitamin B_1 in the infants are depleted. This milk gives a negative peroxidase reaction which becomes positive when the mother is given adequate doses of vitamin B_1. In overfed babies the disease assumes an acute form, in the underfed it tends more to chronicity.

Weiss (p. 283) discusses beriberi as seen in America and Europe where, though the classical forms may be seen, the symptoms are more frequently those of heart disease alone, and are often associated with alcoholism. In these cases thiamin has a marked effect. Walshe (p. 283) discusses polyneuritis, of which beriberi is one cause, and stresses the fact that vitamin B_1 is not antineuritic except in relation to a high carbohydrate diet. He does not believe that polyneuritis is in general due to vitamin deficiency. Fantus *et al.* (p. 284) have discussed subvitaminosis B_1.

SISON and FERMIN (p. 284) give details of a case of beriberi which responded dramatically to thiamin chloride, of which 10 mgm. were injected as the first dose. Details of further treatment are given. SWAN and LAWS (p. 285) describe a case of cardiovascular disturbance, with general oedema, in which the diet had been deficient in vitamin B_1. Treatment with Betaxan was successful. LEONG (p. 285) has estimated the thiamin content of foods available in Malaya.

KARUNAKARAN and NAIR (p. 286) describe a syndrome seen in an asylum in Travancore. This consisted of dermatitis of the scrotal region with stomatitis, follicular keratitis, bleeding from the gums and anaemia. It appears to have been due to polyavitaminosis and was treated with buttermilk, marmite and cod liver oil.

YOUNG and CLARK (p. 286) describe a condition of hypovitaminosis in labourers in East Africa. There was haemorrhage into the muscles of the legs and bleeding of the gums, together with skin changes like those of vitamin A deficiency and of pellagra. *C. W.*

FEHILY (Lydia). **Infantile Beri-Beri in Hong Kong.**—Reprinted from *Caduceus.* Hong Kong. 1940. May. Vol. 19. No. 2. pp. 78–93. [39 refs.] Also in *Jl. Trop. Med. & Hyg.* 1941. Feb. 15. Vol. 44. No. 4. pp. 21–26. [40 refs.]

Japanese workers have shown that the milk and urine of women suffering from beriberi are toxic to infants and mice. The toxic substance consists chiefly of methyl glyoxal. The milk from vitamin B_1-deficient women gives a negative peroxidase reaction, due to inhibition of the reaction by methyl glyoxal; the reaction becomes positive when the mother is given some source of vitamin B_1. The symptoms of infantile beriberi are produced by the toxic milk which is only effective however when the infant becomes depleted of its vitamin B_1 reserves.

In the present investigation 18 per cent. of the infants brought to a Welfare Centre were suffering from beriberi. Of 83 nursing mothers 32 were secreting milk which was peroxidase-negative and 14 of the 32 had symptoms suggestive of adult beriberi. Of the infants of the mothers with peroxidase-negative milk 81 per cent. showed signs of infantile beriberi of varying degrees of severity, but mostly mild. All the affected mothers gave histories of several infantile deaths. After the administration of vitamin B_1 (not less than 500 I.U. daily) the milk showed a positive reaction within a few days. The infants were given, at the same time, 50–500 I.U. daily. In infants the disease was acute, subacute or chronic. The overfed babies developed the acute form, the underfed the subacute or chronic form. Vomiting was a symptom common to all types and cyanosis was always a danger sign. In the acute form the symptoms were those of heart failure with a normal temperature. In the subacute, puffiness of the face, and oliguria occurred, whilst in the chronic form inanition, which might last for weeks, was the prominent sign. The untreated acute form was always fatal. In Hong Kong food prejudice partly accounts for the large incidence of infantile beriberi. Most mothers ascribe their symptoms to "fung" (wind) and therefore abstain from fruits and vegetables. They are less careful about female infants and therefore more males develop beriberi! It is important to note

that "Fung Taam" (wind-mucus) is acute infantile beriberi and is identical with Taon in the Philippines. "Malau gam" (monkey disease) is chronic infantile beriberi. *H. N. H. Green.*

WEISS (Soma). **Occidental Beriberi with Cardio-Vascular Manifestations. Its Relation to Thiamin Deficiency.**—*Jl. Amer. Med. Assoc.* 1940. Sept. 7. Vol. 115. No. 10. pp. 832–839. With 1 chart. [50 refs.] [Summary appears also in *Bulletin of Hygiene.*]

This is a review of clinical and experimental investigations, chiefly by the author and co-workers, on the relation of circulatory disorders to beriberi. Beriberi in both its wet and dry forms occurs regularly in America and Europe and is similar in all its essentials to the disease as seen in the East. The author has observed a large number of cases with "beriberi heart," the chief indications of which are the dietary history, a reduced excretion of thiamin and the clinical response to thiamin chloride treatment. Symptoms of heart disease, when other aetiological factors have been excluded, suggest a search for possible thiamin deficiency as a cause. Excessive alcohol consumption is very commonly associated with beriberi in the Occident, though alimentary disease and dietary restrictions are also factors. It is suggested that the high pneumonia mortality of alcoholics may be in part due to a nutritional deficiency. It has been shown that electrocardiographic changes occur, both in man and animals, given a diet lacking thiamin. The effects observed on the animal heart include tachycardia, bradycardia, cardiac dilatation, congestive failure of the circulation and tissue changes in the myocardium. In the rat the effect does not appear to be due to accumulation of intermediary metabolites, but rather to a direct effect on the metabolism of the heart. There is no explanation yet as to why with a similar diet either dry or wet beriberi may appear, though if polyneuritis first occurs the diminished exertion of the patient will prevent cardiac failure arising. In treatment, large doses of thiamin are given, preferably subcutaneously. If the case is one of beriberi heart, oedema and other lesions clear up fairly rapidly and there is a marked diuresis. Thiamin has no effect on any other type of heart disease. *H. N. H. Green.*

WALSHE (F. M. R.). **Aetiology of Polyneuritis.**—*Lancet.* 1941. Jan. 11. pp. 33–35.

Polyneuritis is a bilateral, symmetrical affection of the peripheral nerve trunks of the limbs, involving both the sensory and motor fibres. The cranial nerves and central nervous system may be affected, and there is always myocardial involvement. Whatever the aetiological agents (of which no more than 10 can certainly be incriminated) there is uniformity of behaviour in all the cases, which suggests that the lesions may be due to a single toxic metabolite. Beriberi is a typical polyneuritis, but it is not certain that B_1 deficiency is responsible for any other form of polyneuritis, though there is good evidence that alcoholic polyneuritis is associated with vitamin B_1 deficiency. Even in beriberi the lesions of the nerve cells are inadequate to account for the type of degeneration seen in the peripheral nerves. It tends to be forgotten that vitamin B_1 is not antineuritic except in relation to a high carbohydrate diet; polyneuritis does not occur, for instance,

in anorexia nervosa. The main features of polyneuritis are qualitatively the same in the acute infection, subacute (*e.g.* diphtheritic) and in the chronic (*e.g.* alcoholic) types. In the author's experience intensive B_1 therapy does not influence acute infective polyneuritis, nor has he seen chronic cases improve more rapidly with B_1 therapy than they did in pre-vitamin days. Treatment still remains as before, with complete rest in bed until the process ceases to progress actively. The author is not a convert to the view that polyneuritis is, in general, due to vitamin deficiency.

[The author does not make it clear whether his chronic cases which showed no response to vitamin treatment included alcoholic cases. This is important because it is the one form of polyneuritis (apart from beriberi) in which there appears to be some agreement as to the value of B_1 therapy.] *H. N. H. Green.*

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. 1940. Aug. 10. Vol. 115. No. 6. pp. 450–454. **The Therapy of Subvitaminosis B_1.** [Edited by Bernard FANTUS, in collaboration with Eugene F. TRAUT & Regina Stolz GREENEBAUM.]

This is an article of "a lecture to students" type, covering well the ground indicated in the title. The authors postulate, as their basis, that subvitaminosis B_1, beriberi and thiamin deficiency are synonymous terms. They then consider circumstances in which this condition is likely to arise, such as inadequate food or an unbalanced diet, inadequate absorption, from disease, relative inadequacy in conditions where the demand is for more than the normal amount (fevers, pregnancy and lactation) and so on. Next, the early premonitory, and the established and late signs are discussed and their diagnostic importance. Finally, treatment, which is divided into prophylactic and therapeutic, and the indications for continuance of treatment, with detailed consideration of the dosage of thiamin to be adopted and the modes of its administration. The advantage of an article such as this is that it deals with the text-book, orthodox aspect, but at the same time gives to the medical public the benefit of wide personal experience. *H. H. S.*

SISON (Agerico B. M.) & FERMIN (Elvira N.). **Spectacular Response to Thiamin Chloride of a Case of Pernicious Beriberi (Shosin).**—*Acta Med. Philippina.* 1940. July–Sept. Vol. 2. No. 1. pp. 1–13. With 1 plate. [10 refs.]

A man of 31 years was admitted to the Philippine General Hospital on account of dyspnoea and general anasarca. His illness had started two years before with palpitation, ready fatigue, dyspnoea and pain in the chest, and, six months later, ascending oedema. The chief physical signs on admission were: pallor of face, visible pulsation in the neck, heart enlarged, no cardiac murmurs, blood pressure systolic 169, diastolic 70. These indicated "hypertensive myocardial disease with congestive failure." Digitalis was given, but, as might have been expected, fruitlessly. The patient became dull and incoherent, the heart took on a gallop rhythm and death seemed to be imminent. It was not till this stage was reached that the idea of beriberi as the cause came to be considered. Thiamin chloride, 10 mgm., was injected and caffeine sodio-benzoate hypodermically, and oxygen

inhalations were started. Improvement set in at once, tiki-tiki extract, 15 cc., was given by mouth. Strychnine was injected for a few days. In five days from the start of thiamin the oedema had almost disappeared, dyspnoea and polypnoea had cleared up; there was some ascites, but this too passed. After receiving a total of 100 mgm. of thiamin chloride intramuscularly and 150 mgm. intravenously, the patient was able to be up and about, but knee-jerks were still absent, there was diminution of motor power, and inability to rise unaided from a sitting posture. Thiamin was discontinued, Betaxan given instead (2 mgm. intravenously for 33 days). When leaving hospital he still had absent knee-jerks, somewhat slow mentality (but the state of this before admission could not be ascertained, as the patient's relatives could not be communicated with). *H. H. S.*

SWAN (W. G. A.) & LAWS (F.). **A Case of Beriberi Heart.**—*Brit. Heart Jl.* 1940. Oct. Vol. 2. No. 4. pp. 241–246. With 3 figs.

[The title of this paper is misleading. The title of the preceding article in this journal would have been more appropriate, *viz.* Cardiovascular Disturbances caused by Deficiency of Vitamin B_1, for this patient did not show the symptoms typical of beriberi.]

The case here recorded is that of a man, aged 55, who from poverty had only 9 shillings a week to live on after paying his rent. His diet consisted of white bread, 4 rounds a day, or four 2½d. loaves a week, 2 boiled eggs, 8 oz. tinned milk, potatoes, sausage meat and beer 1½ pints, together yielding only 819 I.U. of vitamin B_1 in the week.

He presented general oedema, but no respiratory distress when he was at rest, deep reflexes were active, there was no alteration of sensation, in fact no neuritic symptoms at all. The pulse was regular, not unduly fast, the diastolic pressure not low and the pulse pressure about normal. The liver was neither enlarged nor tender.

Betaxan was given and after 24 hours the urinary output increased (160 oz. on the fifth day), the oedema subsided and in ten days he felt quite well. The vitamin was continued in 2 mgm. doses (he received altogether 32 mgm.) and he left hospital 2 months after admission, free of symptoms. *H. H. S.*

LEONG (P. C.). **Vitamin B_1 (Thiamine) Content of Foods.**—*Jl. Malaya Branch Brit. Med. Assoc.* 1940. June. Vol. 4. No. 1. pp. 66–107. With 3 charts. [33 refs.] [Summary appears also in *Bulletin of Hygiene.*]

This article cannot be abstracted, but is of great value for reference. The author has estimated the thiamin content of foods available in Malaya, dividing them into ten groups: 1. Cereals and pulses and their products (47); 2. Fruits (67); 3. Nuts and oil seeds (19); 4. Greens, roots and other vegetables (86); 5. Milk and milk products (20); 6. Eggs (7); 7. Meat and meat products (36); 8. Fish and other marine products (34); 9. Poultry and game (14); 10. Miscellaneous, including bird's nest, coriander, gingelly oil, honey, sago, tamarind, treacle, yeast (15).

Other tables show the effect of cooking on the thiamin content of 15 foods boiled in water for 10 minutes, 23 boiled for 20 minutes and 5 for 30 minutes, and of 12 others fried in coconut oil for 10 minutes.

The reduction in vitamin B_1 might be very great (up to 80 per cent. in the case of lettuce boiled for 10 minutes) or it might be nil. An instructive discussion of each of these groups follows. *H. H. S.*

VEDDER (E. B.). **Beriberi and Vitamin B_1 Deficiency.**—*Amer. Jl. Trop. Med.* 1940. Sept. Vol. 20. No. 5. pp. 625–640. [37 refs.]

JOLLIFFE (Norman). **Recent Advances in Clinical Applications of the B-Vitamins.**—*Jl. Amer. Dietetic Assoc.* 1941. Jan. Vol. 17. No. 1. pp. 5–11. [17 refs.]

KARUNAKARAN (C. O.) & NAIR (P. Krishnan). **The Treatment of Scrotal Eczema, Stomatitis and Allied Conditions caused by Vitamin Deficiency.**—*Indian Jl. Med. Res.* 1940. Oct. Vol. 28. No. 2. pp. 371–383. With 5 figs. on 2 plates. [21 refs.]

The authors record observations made upon the treatment of an affection which broke out in a large asylum at Travancore. The chief complaint was a dermatitis involving mainly the scrotum, the groins, and penis; this was associated with angular stomatitis, glossitis, follicular keratitis (phrynoderma) and xerophthalmia in many cases, also bleeding from the gums and anaemia in some proportion, and, in a few, burning sensations in the palms and soles. In none were there signs of nerve lesions, diarrhoea, or dermatitis on the limbs. In a few the mucocutaneous junction of the prepuce was affected.

This syndrome will be recognized as resembling those which have been described now many times, and reported in this *Bulletin*. Ninety-two cases in all came under observation [what proportion of the asylum population is not stated], scrotal eczema was present in 81, angular stomatitis in 60, glossitis in 58, phrynoderma in 29, xerophthalmia in 27, bleeding from the gums in 27. For the purposes of evaluating treatment, cases were divided into groups and transferred from one group to another as necessary. The results are shown in a number of tables which cannot be reproduced here and which it is impossible to condense.

The general conclusions are that "the sore mouth is due *almost* wholly to the deficiency of the vitamin B_2 factor" while "the scrotal eczema appears to be a polyavitaminosis."

The best all-round results for all five symptoms in the complex appear to have been obtained with buttermilk or with marmite and codliver oil at the same time. The authors think one factor may have an adjuvant action upon another. *H. S. Stannus.*

YOUNG (W. A.) & CLARK (E. Malcolm). **Report of a Small Epidemic of Hypovitaminosis.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1940. Nov. 30. Vol. 34. No. 3. pp. 249–260.

In this interesting article the authors describe what they call a small "epidemic" of hypovitaminosis. Their cases numbered thirty-one and the outbreak occurred among adult male African natives recruited three to four months previously near Kisumu on Lake Victoria Nyanza, employed as labourers on road-making in a dry semi-desert country where the diet provided was very foreign to that they usually enjoyed. [Of the actual incidence of the affection no mention is made.] The symptom for which these men sought treatment was an

inability or reluctance to walk, interpreted by the observers as due to stiffness, weakness and a desire to avoid pain. Examination showed swelling and induration in some one or more groups of muscles in the calf of one or both legs, or in the muscles of the front or back of the thigh, associated with a hot shiny superjacent skin but no true oedema. The condition was afebrile. Exploration of the affected part revealed a haemorrhagic condition involving the muscle; it was "difficult to distinguish between muscle tissue and blood clot." The condition is referred to [wrongly in the light of the further observation] as a myositis. The lower limbs only were affected, in a few cases a bloody effusion into a joint was noted and in one a haemothorax. The gums which at first were considered to be healthy were later discovered to bleed easily.

The second point of interest common to the majority of these cases was the occurrence of some affection of the skin, including the follicular hyperkeratosis commonly ascribed to a vitamin A deficiency, dryness and general hyperkeratinization, a mosaic appearance with hyperpigmentation of the skin of the legs and thickening with wrinkling and hyperpigmentation of the skin over the knees, ankles, knuckles, etc., conditions not uncommon in pellagra. There was, however, no night blindness nor xerophthalmia on the one hand, and no sore mouth, no glossitis and no gastrointestinal disturbance on the other. No albuminuria, but bradycardia and exaggerated knee jerks were noted. The cogent fact than an outbreak of scurvy occurred among native troops stationed in the same district in 1928 is mentioned. [The authors have added one more to the many accounts now recorded of conditions occurring among native races due to nutritional deficiencies. Scurvy may at any time present a puzzling picture when first met with, more especially if for diagnosis text-book descriptions of the disease are depended on. It is disappointing to find no references to treatment.]

H. S. S.

PALLISTER (R. A.). **Some Observations on Food Deficiency Diseases in Malaya.**—*Jl. Malaya Branch Brit. Med. Assoc.* 1940. Sept. Vol. 4. No. 2. pp. 191–197.

EPIDEMIC DROPSY.

PRÉCIS OF ABSTRACTS IN THIS SECTION.

In an account of a comprehensive investigation, LAL *et al.* (p. 288) show that the seeds of *Argemone mexicana* are to be found, in varying proportions, in many stocks of mustard seed in India. They conclude, from careful estimations, that oil containing less than one per cent. argemone oil, or oil representing 1 mgm. of the reacting substance, taken daily for 20 days, is not likely to produce clinical symptoms.

SEN GUPTA and NAPIER (p. 289) give details of the haematological changes in epidemic dropsy. *C. W.*

LAL (R. B.), MUKHERJI (S. P.), DAS GUPTA (A. C.) & CHATTERJI (S. R.). **Investigations into the Epidemiology of Epidemic Dropsy. Part IX. Quantitative Aspects of the Problem of Toxicity of Mustard Oil.**—*Indian Jl. Med. Res.* 1940. July. Vol. 28. No. 1. pp. 163–196. With 2 graphs.

This is an account of one of the most important of the investigations undertaken by the authors to elucidate the aetiology of epidemic dropsy. In this contribution they consider three questions: 1. To what extent seeds of *Argemone mexicana* are actually found in stocks used for pressing oil. 2. Whether a quantitative test could be developed to express the amount of toxic substance in terms of argemone oil in a sample of mustard oil. 3. How much toxic substance must be ingested to produce clinical symptoms.

To determine the first of these they obtained samples of the mustard seed daily from a certain oil mill in Calcutta and found that three of the samples of *Brassica juncea* contained 5 per cent. of Argemone seed. Rarely was a sample found to contain one variety only of seed; the name is given to the predominant type. In another series of samples from different oil mills and stocks of seeds from wholesale dealers, amounts of the Argemone seed might constitute 10 per cent. or more. The experiments directed towards determining the second question were of too intricate a nature for abstract, and anyone wishing to repeat and confirm them should consult the original. The conclusion of the authors is that "the form in which the reacting substance exists in the oil is not identical with the pure crystalline substance, and the key to the nature of the toxin may be hidden here."

Investigations carried out into an epidemic at Satkhira show that many escaped because the amount consumed was just below that causing symptoms. Generally speaking, "the presence of less than 1 per cent. of Argemone oil in mustard oil will fail to cause demonstrable symptoms of epidemic dropsy under reasonably average conditions of mustard oil consumption in Bengal."

The contents of this valuable contribution cannot be expressed better than in the authors' own words as given in their summary:—

"1. It has been shown that many stocks of mustard seed, particularly those of *B. juncea* found in oil mills, contain variable amounts of argemone seed. In some of these supplies the proportion of argemone seed, though sufficient to give rise to positive results with nitric acid tests in the oil expressed from them, may not be enough to cause symptoms of the disease. It is therefore a question whether a wholesale rejection of such supplies would be justifiable and whether it would not unnecessarily dislocate business. Quantitative aspect of the problem, therefore, assumes a considerable importance.

"2. A colorimetric quantitative test has been developed and gauging curves have been worked out from which milligrams of the reacting substance per 100 cc. of oil and roughly the percentage of argemone oil can be directly read off against the colorimetric (Pulfrich) reading.

"3. It has been shown that light and air reduce the reacting-substance content of mustard oil containing argemone oil.

"4. While light is necessary for this reaction, presence of air is not essential in the case of mixtures of argemone oil in mustard oil. It is, however, necessary in the case of pure argemone oil.

"5. Both the visible and ultra-violet radiations act equally well in reducing the reacting-substance content of the oil. Direct light gives quicker results than diffused light.

"6. Heat is not concerned in this reaction.

"7. Attempt has been made to determine the minimum quantity of argemone oil in mustard oil, the consumption of which will produce symptoms. The problem has been tackled in various ways, namely, comparison of the toxic effects, as suggested by the epidemiological histories, with the reacting-substance contents of the oil, tracing an oil containing known amount of reacting substance to the consumers and observing developments amongst them, concurrent study of the oil and of the persons consuming it and finally determining the reacting substance of samples of oil used in human feeding experiments.

"8. All these studies point to the conclusion that oil containing less than one per cent. argemone oil, or oil representing 1 mg. of the reacting substance taken daily for 20 days, is not likely to produce clinical symptoms."

H. H. S.

SEN GUPTA (P. C.) & NAPIER (L. Everard). **Haematological Changes in Epidemic Dropsy.**—*Indian Jl. Med. Res.* 1940. July. Vol. 28. No. 1. pp. 197–206.

Previous studies on the blood in epidemic dropsy gave varied results so the present research was done with standard methods on Calcutta labourers, and the data were compared with those known standards for Indian population. The nature of the anaemia, the sedimentation rate and leucocyte changes were examined. The first included Hb. content, red cell count, reticulocyte percentage, van den Bergh test, total cell volume, and calculation of mean corpuscular volume, mean corpuscular Hb., and mean corpuscular Hb. concentration. Of 11 males, 2 were slightly macrocytic, 1 slightly microcytic and 8 normocytic; of 11 females 3 were slightly macrocytic, 2 microcytic and 6 normocytic. The average case was orthochromic and normocytic or slightly macrocytic. The indirect van den Bergh was negative and there was no reticulocytosis, *i.e.*, there was no evidence of excessive blood destruction. This, combined with the results of sternal punctures in 3 cases, indicated that the anaemia was due to depressed erythropoiesis. The sedimentation rate (Westergren) was above normal in all of 34 cases, and when the correction for anaemia was made in 21 cases the rate was still increased in 70 per cent. of the cases, indicating that some factor was operative in addition to anaemia. The white cell count was usually normal but was occasionally a little high. The differential count did not differ much from normal, but there was a "shift to the left" of the neutrophils. *W. P. Kennedy.*

MALARIA.

PRÉCIS OF ABSTRACTS IN THIS SECTION.

RAMAN (p. 290) claims to have found a *P. ovale* infection contracted in India.

WOLFF (p. 291) gives details of a simplified technique for his buffer precipitation test for the diagnosis of chronic malaria.

REED (p. 291) has written a general article on the treatment of malaria. LYNCH and BRANDT (p. 291) report a case of quinine poisoning in a child. STEPHENSON (p. 292) reports success in the treatment

of malarial splenomegaly by the Ascoli method. Splenomegaly due to kala azar was slightly reduced in three cases, but the treatment had no effect on enlarged spleens due to bilharzia or to unknown causes.

HENDERSON and HOWARD (p. 292) have compared a Paris green mixture with a pyrethrum emulsion as a larvicide. The latter is no more efficient than the former, costs much more and in the work reported killed numerous invertebrate mosquito predators. BISHOP (p. 292) records observations made in the Tennessee valley, where there has been a change from river to lake conditions, and where Paris green, larvicide oil, and pyrethrum larvicide have been used in mosquito control. The effects of these on fish, aquatic organisms and vegetation are mentioned.

TWEEDIE (p. 293) writes of the value of fascine drainage, especially for rubber estates.

Malaria of monkeys and birds.—By incubating *P. knowlesi* with the serum of human beings who had recovered from a *P. knowlesi* infection, and by using normal serum as a control, and injecting these mixtures into monkeys, COGGESHALL (p. 293) has produced evidence of definite immune bodies in the serum of recovered patients, which rendered the parasites almost or completely harmless to the animals. Complement fixing antibodies were also found but were not apparently correlated with the protective action of the serum. SINGH and SINGH (p. 294) report success in the treatment of *P. knowlesi* infection in monkeys by means of immune serum from chronically infected animals. They (p. 294) show that *P. knowlesi*, *P. cynomolgi* and *P. inui* produce immunity against reinfection with the same species, but not against each other, in monkeys. They further (p. 294) found that only anti-*P. knowlesi* serum caused agglutination of red cells infected with that parasite.

From experimental work, SCHULEMANN and SPIES (p. 294) show that pigment-free exoerythrocytic schizonts of *P. gallinaceum* which arise directly from sporozoites, like those which develop from pigmented erythrocytic forms, are found in histiocytes. Further development is stated to take place either extracellularly, or intracellularly, giving rise to exoerythrocytic schizonts or to the ordinary pigmented stages found in red blood cells. HEWITT (p. 295) concludes from his work on *P. cathemerium* that if exoerythrocytic schizogony is part of the life cycle of some avian parasites, the factors governing its appearance are unstable. One strain of parasite may be associated with these bodies while they may be entirely absent in another strain.

HEGNER (p. 296) has found that *P. cathemerium* does not multiply in the blood of canaries to the extent which its normal merozoite production would imply, and argues that an increasing percentage of parasites is destroyed each day, indicating that immunity is acquired gradually. *C. W.*

RAMAN (T. K.). *Plasmodium ovale* **in India.**—*Jl. Indian Med. Assoc.* 1940. Sept. Vol. 9. No. 12. pp. 583–585. With 6 figs.

This is a description of a case of malaria and of the parasites found in the peripheral blood. The patient was infected somewhere in India. The author states that the parasite had all the appearances of *P. ovale*. The microphotographs produced do not justify a definite opinion. It was a mixed infection, as occasional crescents were found. *Norman White.*

WOLFF (E. K.). **The Buffer Precipitation Test for Malaria (B.P.T.) adjusted for Large-Scale Examinations.**—*Indian Med. Gaz.* 1940. Sept. Vol. 75. No. 9. pp. 517–519.

The author's buffer precipitation test for the diagnosis of chronic malaria infection has already been described [see this *Bulletin*, 1940, Vol. 37, p. 57]. A further simplified technique, which gives satisfactory results, is now described. Only two tubes are used for each test, one containing 1 cc. of the test solution and the other 1 cc. of the control solution. These solutions are made up as follows :—

Test solution

Stock buffer solution *p*H 7·7 ...	one part
Glass-distilled water	four parts
Formalin	0·2 per cent.

Control solution

Stock buffer solution *p*H 7·0 ...	one part
Glass-distilled water	four parts
Normal saline	five parts
Formalin	0·2 per cent.

Two drops of serum are placed in each tube. The reading may be done after the lapse of from half-an-hour to two hours and is based on the comparison of the two tubes. The reading is best done by daylight. The value of negative tests is high if the blood be taken at the right time, preferably in the morning before breakfast : the acute feverish period of a malaria attack should be avoided. *N. W.*

REED (Alfred C.). **The Treatment of Malaria.**—*Jl. Amer. Med. Assoc.* 1940. Aug. 24. Vol. 115. No. 8. pp. 602–605.

This is one of a series of articles written by eminent authorities for the purpose of extending information concerning the official medicines. In it the treatment of malaria is adequately described in small space. Most attention is devoted to the use of quinine salts, plasmoquine and atebrin. Other drugs for which antimalarial properties have been claimed have not escaped notice and some useful information on symptomatic treatment is included. The author pays due regard to the importance of developing and maintaining immunity, which is at times the best of all treatments, but in *P. falciparum* infections there is constant clinical danger as long as the patient harbours plasmodia. With regard to the treatment of chronic malaria and malarial cachexia the author states " NOCHT and MAYER recommend a mixture of plasmochin and quinine sulfate for twenty-one days by mouth, *three tablets after each meal*. . . . Each tablet contains 0·01 gm. of plasmochin and 0·03 gm. of quinine sulfate." This appears to be a misprint : the words italicized should read " three to four tablets daily after meals, usually 3 tablets suffice " [NOCHT, B. and MAYER, M. *Malaria.* John Bale, 1937, p. 59.] Elsewhere in the article the author rightly insists that plasmoquine should never be given in a dosage exceeding 0·065 gm. (1 grain) by mouth a day. *N. W.*

LYNCH (P. P.) & BRANDT (C. W.). **Quinine Poisoning. Report of a Fatal Case.**—*New Zealand Med. Jl.* 1940. Aug. Vol. 39. No. 212. pp. 191–194.

A child, one year and eight months old, got possession of a bottle of quinine bisulphate tablets and swallowed a number. The total

quantity of quinine taken by the child was at least 50 grains and may have been as much as 100 grains. Attempts at making the child vomit failed. The child became restless, twitching commenced, his lips went blue, the body became limp and he died about two hours after he had been found with the bottle. Post mortem no tablets were found in the stomach but in the upper three or four feet of the small intestine the remains of ten tablets were found in various stages of disintegration.

N. W.

STEPHENSON (R. W.). **Treatment of Splenomegaly by Ascoli's Method.** —*Lancet.* 1940. Nov. 23. pp. 648–649.

A series of 18 cases, in all of which the spleen extended to, or below, the umbilicus, was treated by Ascoli's method. Chronic malaria was the cause of the splenomegaly in 11 cases ; three were cases of kala azar, one of bilharzia. No cause for the splenomegaly could be found in three cases. Nine of the 11 malaria cases improved greatly ; in these the spleen was either not palpable at the end of treatment or could only just be felt below the costal margin. There was also considerable improvement in the general condition. One of the two patients in whom the treatment was unsuccessful suffered from mitral stenosis. The three patients with splenomegaly of unknown cause derived no benefit from the treatment. There was slight reduction in the size of the spleen in one of the kala azar cases. The splenomegaly of the bilharzia case was unaffected by the treatment.

N. W.

HENDERSON (John M.) & HOWARD (R. S.), Jr. **A Comparative Evaluation of Paris Green and Pyrethrum Emulsion as Anopheline Larvicides in Georgia : a Progress Report.**—*Amer. Jl. Trop. Med.* 1940. July. Vol. 20. No. 4. pp. 585–592.

The Paris green mixture used in these experiments consisted of Paris green (not less than 50 per cent. arsenious oxide) 10 parts, and ordinary builder's lime 90 parts. The pyrethrum emulsion had the following composition :—pyrethrum extract (2 per cent. pyrethrins) 0·25 gals. ; 40 per cent. liquid potash soap 0·25 gals. ; white kerosene 4·75 gals. ; water 2·25 gals. It was found that an application rate of something over 3 gallons of undiluted pyrethrum larvicide per acre is necessary to cause anopheline mortality equivalent to that produced by applying 0·5 lb. of Paris green per acre. The cost of pyrethrum larvicide was from ten to fifteen times that of the Paris green mixture required to produce equivalent larval mortality. The pyrethrum emulsion killed or injured numerous invertebrate mosquito predators.

N. W.

BISHOP (E. L.). **Cooperative Investigations of the Relation between Mosquito Control and Wildlife Conservation.**—*Science.* 1940. Aug. 30. Vol. 92. No. 2383. pp. 201–202.

There has been a change from river to lake conditions in the Tennessee valley resulting in certain major biological readjustments within the area. Various interested bureaux and services met and decided to investigate conjointly the possible conflict between malaria control procedures and wildlife conservation. Field studies were begun during the summer of 1939. The continuous fluctuation of

water level for anopheline control, and the fluctuations for flood control and navigation, made it difficult to separate the influence of these factors from one another and from other malaria control procedures. Variation of water level produces changes in the aquatic vegetation and has a marked effect upon the qualitative and quantitative distribution of aquatic organisms. Paris green applied by aeroplane at the rate of about one pound per acre had no deleterious effect upon vegetation and produced no catastrophic destruction of aquatic organisms important as fish food. Arsenical residues accumulate in the bottom of the reservoirs in variable amounts. Arsenic accumulates also in the fish but in quantities insufficient to be a menace to human consumption. Fish from these reservoirs gave evidence of disturbed metabolism. Larvicidal oil and pyrethrum larvicide destroy a large proportion of amphipods. These interesting joint studies are to be continued and extended in scope. *N. W.*

TWEEDIE (D. Reid). **Fascine Drainage as an Anti-Malaria Measure.**—*Jl. Malaya Branch Brit. Med. Assoc.* 1940. Sept. Vol. 4. No. 2. pp. 167–171. With 9 figs. on 2 plates & 2 text figs.

The author is an enthusiastic advocate of fascine drainage. He describes and illustrates the method he adopts in carrying it out. It is simple, cheap, efficacious and semi-permanent. For rubber estates he regards it as superior to subsoil piping because of its simplicity and economy; choking with roots of trees does not seem to occur.

N. W.

COGGESHALL (L. T.). **The Occurrence of Malaria Antibodies in Human Serum following Induced Infection with** *Plasmodium knowlesi*.—*Jl. Experim. Med.* 1940. July 1. Vol. 72. No. 1. pp. 21–31. [12 refs.]

In this paper the author describes experiments in which serum from human beings who had recovered spontaneously from therapeutic *Plasmodium knowlesi* infections was tested for protective properties against infections with this parasite in monkeys. The procedure was to incubate 2 cc. of the serum with 10,000 parasites for half an hour at 37°C. and then to inject the mixture intraperitoneally into monkeys. In some cases the number of parasites incubated with the serum was increased to 100,000 and to 1,000,000. As a control, incubation with normal serum was carried out. The results of these inoculations into monkeys were that the infections resulting after use of normal serum ran acute courses ending fatally, whereas after serum from recovered patients no infection occurred or the infections were so modified that recovery occurred. There can be no doubt that definite immune bodies occur in the serum of individuals who have recovered from *P. knowlesi* infections. It is pointed out, however, that the demonstration of the presence of such bodies is more difficult than in the case of bacterial immune bodies, for malarial parasites are, during stages of growth, protected by the red blood corpuscles and that it is only in the adult stages, when the enclosing red blood cells have been damaged, that immune bodies can have an effect.

In addition to the protection tests, complement fixation tests were carried out. All convalescent sera tested gave evidence of the presence of complement-fixing antibodies but there was no uniform correlation between their titre and the protective action of the sera.

C. M. Wenyon.

SINGH (Jaswant) & SINGH (Harwant). **Passive Immunity in Monkey Malaria.**—*Jl. Malaria Inst. of India.* 1940. June. Vol. 3. No. 1. pp. 137–142. With 1 chart. [14 refs.]

Attempts were made to modify the course of *Plasmodium knowlesi* infections in *M. rhesus* by the administration intraperitoneally or intravenously of immune serum from chronically infected animals. Some monkeys which first received serum after the infection had become well established were successfully treated, but early treatment with relatively large doses commencing from the day of inoculation appeared to give better results. *C. M. W.*

SINGH (Jaswant) & SINGH (Harwant). **Observations on Immunity in Monkey Malaria as evidenced by the Results of Superinfections.**—*Jl. Malaria Inst. of India.* 1940. June. Vol. 3. No. 1. pp. 99–114. [36 refs.]

M. rhesus which had recovered from infections due to *Plasmodium knowlesi*, *P. cynomolgi* or *P. inui* were re-inoculated with one or other of these parasites at varying intervals. It was found that a chronic infection with any one of these parasites did not prevent or modify the course of reinfection with a different parasite but did prevent re-infection with the same parasite. In the case of *P. knowlesi* the immunity to reinfection appeared to diminish four months after disappearance of parasites from the peripheral blood. In the case of the other two parasites immunity was effective for at least 11 to 18 months. *C. M. W.*

SINGH (Jaswant) & SINGH (Harwant). **Agglutination Reactions with** *Plasmodium knowlesi.*—*Jl. Malaria Inst. of India.* 1940. June. Vol. 3. No. 1. pp. 53–66.

A washed suspension of red blood corpuscles from *M. rhesus* infected with *Plasmodium knowlesi* was employed, as recommended by EATON (1938), as an antigen in agglutination tests with sera from other monkeys which had recovered from acute infections with *P. knowlesi*, *P. inui* or *P. cynomolgi*. It was found that the *P. knowlesi* sera alone caused clumping of the infected red cells of the antigen. The intensity of the reaction depended chiefly upon the sensitiveness of the antigen and duration of the infection. Fresh antigens alone were suitable for the test, as with keeping deterioration occurred. *C. M. W.*

SCHULEMANN (W.) & SPIES (K.). Zu Ursprung und Entwicklung der pigmentfreien Formen der Malaria-Parasiten. [**Origin and Development of Pigment-Free Forms of Malaria Parasites.**]—*Deut. Med. Woch.* 1940. Apr. 12. Vol. 66. No. 15. pp. 404–405.

In a previous publication [this *Bulletin*, 1941, Vol. 38, p. 35] the first author has shown that the cells which ingest colloidal palladium,

and which are therefore histiocytes, are those in which develop the exoerythrocytic schizonts of *Plasmodium gallinaceum* which are found to occur after injection of the pigmented erythrocytic stages of the parasite into fowls. The early stages of these schizonts appear to be identical with the first developmental stages of sporozoites as described by KIKUTH and MUDROW. The cells in which the sporozoites developed were designated monocytic cells by these authors. It seemed, to the authors of the paper under review, of interest to determine the exact nature of these cells. Accordingly a technique devised by KIYONO to produce local aggregation of histiocytes was adopted. This consisted in implanting under the skin of the wing of fowls sterile pieces of sponge which has the property of bringing about the required aggregation of the histiocytes. Eight to ten days after the operation a piece of the resulting growth is excised and examined. If it is found to consist chiefly of histiocytes a suspension of sporozoites in equal parts of chicken serum and 0·9 per cent. saline is injected into the growth. Before this injection, however, a subcutaneous injection of either dianil violet BE or colloidal palladium is given. This has the property of blocking the histiocytes. At varying intervals after the injection of sporozoites portions of the growth are excised and teased and preparations made. These are stained by Giemsa stain. Twenty-four hours after the injection four-nuclear stages, both intracellular and extracellular, are found. After 40 or 65 hours beside the four-nuclear stages which can still be detected are larger forms with large numbers of nuclei. This development is in agreement with the description of Kikuth and Mudrow. It was also noted that when these schizonts were intracellular the cells containing them included also granules of the dianil violet or palladium. There can thus be no doubt that the pigment-free exoerythrocytic schizonts which arise directly from sporozoites, like those which develop from the pigmented erythrocytic forms when these are injected into fowls, are contained in histiocytes. According to MISSIROLI, between the actual sporozoites and the small four-nuclear stages there are earlier developmental extracellular forms. Further development takes place either extracellularly or intracellularly. The intracellular development is either in histiocytes, giving rise to the well-known pigment-free exoerythrocytic schizonts, or in erythrocytes, when the pigmented stages are formed. The authors state that they are carrying out further studies by means of sections in place of smears in order to determine the exact position of the developmental forms in relation to the cells.

C. M. W.

HEWITT (Redginal). **Exo-Erythrocytic Bodies in Canaries infected with a Mexican Strain of** *Plasmodium cathemerium.*—*Amer. Jl. Hyg.* 1940. May. Vol. 31. No. 3. Sect. C. pp. 61–66. With 2 figs. [16 refs.]

The paper reports that *Plasmodium cathemerium* was discovered in the blood of a finch purchased in Mexico City. A canary was inoculated with blood from the finch, an infection resulting. On the ninth day the organs of the canary were examined for exoerythrocytic bodies but none was found. They were found, however, in large numbers in the spleen, liver and bone marrow of one of two canaries infected

from the first canary. From the bird which showed the exoerythrocytic bodies four other canaries were inoculated but only two of these were positive for the bodies. In one of the negative birds, however, a parasite which has been variously styled haemogregarine or toxoplasm was found in monocytes in the liver and spleen. Though the parasite was of the same type as one which had been found in the original finch which harboured the malarial parasite, it is concluded that the infection in the canary had not originated from that of the finch but had been present before it was inoculated with the malarial parasite. The author remarks that if the exoerythrocytic schizogony is part of the life cycle of some avian malarial parasites the factors which govern its appearance are evidently unstable. It is noted that such schizonts have never been found in another strain of *P. cathemerium* which has been carried through hundreds of passages since 1936. A particular search for them has been made without result in organs of 150 of the birds. It seems that one strain of a parasite may be associated with the bodies while in another strain of the same parasite they are entirely absent. *C. M. W.*

HEGNER (Robert). **A Note on the Development of Acquired Immunity in Avian Malaria.**—*Amer. Jl. Hyg.* 1940. July. Vol. 32. No. 1. Sect. C. pp. 24–26. With 1 fig.

Working with *Plasmodium cathemerium* in canaries, the author has found that, according to the average number of merozoites produced at schizogony, which is 13, there should be, theoretically, a thirteenfold increase in the number of parasites in the blood each day. This is far from being the case, for if a sufficient inoculation of infected blood is injected into a canary to give rise to the immediate presence of parasites in the blood, on the following day there may be 60 parasites for every 10,000 red cells. On the next day the figure has risen to only 410 instead of to 780 (60 × 13) and on the succeeding day to 800. It is thus observable that an increasing percentage of parasites is destroyed each day, as shown by such a series of percentages as 47·7, 85·0, 89·5, 94·4, 91·5, 94·8, 96·5, 97·8—a sequence of events which indicates that the immunity is acquired gradually and does not appear suddenly at the crisis. Human and monkey malaria appears to be similar to that of birds in this respect. *C. M. W.*

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